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CARCINOGENESIS ABSTRACTS

VOLUME 8

151
1970

CONTENTS

	<u>PAGE</u>
Review	1, 33, 73, 117, 199, 279, 325, 399
Physical Carcinogenesis	3, 34, 74, 121, 204, 281, 329, 405
Chemical Carcinogenesis	6, 35, 75, 123, 208, 283, 333, 410
Viral Carcinogenesis	16, 54, 91, 153, 239, 299, 367, 442
Epidemiology and Biometry	25, 67, 109, 177, 258, 312, 389, 483
Miscellaneous	29, 70, 115, 191, 271, 323, 397, 506
Author Index	514
Subject Index	538

Prepared by Scientific Literature Corporation
(A subsidiary of the 3i Company)
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Pursuant to a Contract with the Public Health Service
U.S. Department of Health, Education and Welfare
PH43-70-2036

Use of funds for printing this publication approved by
the Director of the Bureau of the Budget on July 25, 1967.

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JANUARY 1970

Abstract Nos. 1-160

Vol. 8

No. 1

CARCINOGENESIS ABSTRACTS

National Cancer Institute

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE • National Institutes of Health

CARCINOGENESIS ABSTRACTS

Volume 8, Number 1
January, 1970

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CONTENTS

	<u>Page</u>
Review	1
Physical Carcinogenesis	3
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Viral Carcinogenesis	16
Epidemiology and Biometry	25
Miscellaneous	29
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The National Cancer Institute, in response to Congressional interest and desire for a national program of cooperative research in cancer, is establishing a means whereby information in the field of carcinogenesis will be coordinated and made available. The information to be included will be obtained from the National Cancer Institute, other governmental agencies, and non-governmental research institutions.

The issuing of Carcinogenesis Abstracts under the auspices of the National Cancer Institute will provide a central source for current abstracting of the carcinogenesis literature being published throughout the world. This will help facilitate an integrated and cooperative program of investigation in this area. The growing number of publications in the area of carcinogenesis makes imperative the availability of an appropriate abstracting service so that investigators may be apprised of progress with a minimum of delay. It is our desire to provide the investigator with a readily systematized compilation of the published work.

Carcinogenesis Abstracts will be published monthly and will include abstracts from the most recently published literature.

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NOTE

Journal names are abbreviated according to the list of abbreviations used by Index Medicus. If the journal is not covered by Index Medicus, then the abbreviations (with some modifications) found in World Medical Periodicals, 3rd Edition, are used.

ABBREVIATIONS USED IN ABSTRACTS

admin.	administered, administration	mg	milligram(s)
av.	average	min.	minute(s)
C	curie(s)	ml	milliliter(s)
mC	millicurie(s)	mm	millimeter(s)
μC	microcurie(s)	mo.	month(s)
cm	centimeter(s)	MTD	maximum tolerated dose
conc.	concentration	NIH	National Institutes of Health, USA
cpm	counts per minute	p.o.	orally
DNA	deoxyribonucleic acid	QO ₂	oxygen quotient
DNase	deoxyribonuclease	PFU	plaque forming unit
e.g.	for example	ppm	parts per million
FFU	focus forming unit	pt.(s)	patient(s)
g.i.	gastrointestinal	RBC	red blood cells (erythrocytes)
g	gram(s)	RES	reticuloendothelial system
μg	microgram(s)	resp.	respectively
Hb	hemoglobin	RNA	ribonucleic acid
i.a.	intra-arterial	RNase	ribonuclease
ID ₅₀	median infectious dose	soln.	solution
inj.	injected, injection(s)	s.c.	subcutaneous
inoc.	inoculated, inoculation(s)	TCID	tissue culture infectious dose
i.p.	intraperitoneal	x	times (e.g. x 3/wk.)
I.U.	international unit(s)	U	unit
i.v.	intravenous	UV	ultraviolet
kg	kilogram(s)	vol.	volume
LD ₅₀	median lethal dose	VA	Veterans Administration
M	molar, mole(s)	wt.	weight
mM	millimole(s)	WBC	white blood cells (leukocytes) or white blood cell count
μM	micromole(s)		
max.	maximum	yr.	year(s)

LANGUAGE ABBREVIATIONS

Af.	Afrikaans	E.	English	Hun.	Hungarian	Lith.	Lithuanian	Ser.	Serbo-Croatian
Ar.	Arabic	Eston.	Estonian	ic.	Icelandic	Maced.	Macedonian	Sl.	Slovene
Bul.	Bulgarian	Fin.	Finnish	In.	Indonesian	Nor.	Norwegian	Sp.	Spanish
Ch.	Chinese	Fr.	French	It.	Italian	Pol.	Polish	Sw.	Swedish
Cz.	Czech	Ger.	German	Jap.	Japanese	Por.	Portuguese	Th.	Thai
Dan.	Danish	Gr.	Greek	Kor.	Korean	Rum.	Rumanian	Uk.	Ukrainian
Dut.	Dutch	Heb.	Hebrew	Latv.	Latvian	Rus.	Russian	Viet.	Vietnamese

- 70-1 ABNORMAL ESTROGEN METABOLISM AND TISSUE ESTROGEN RECEPTOR PROTEINS IN BREAST CANCER. (E.) Lemon, H. M. (U. Nebraska Coll. Med., Omaha). Cancer 25(2):423-435, 1970. (78 references)

The relationships of the relative conc. of estradiol and estriol (the principal "impeded" estrogen in man) to mammary tumor induction and development in rats, and the epidemiology of breast cancer in women, are discussed.

- 70-2 THE PROBLEM OF POSSIBLE EFFECTS OF ORAL CONTRACEPTIVES ON CANCER OF THE BREAST. (E.) Hertz, R. (Rockefeller U. Population Council, New York, N. Y.). Cancer 24(6): 1141-1145, 1969. (52 references)

Since most studies of estrogen (E) carcinogenesis in animals deal with the effects of E alone, rather than the effects of combinations of E + progestational hormones (PH), and since most epidemiologic studies of breast and genital cancer in women taking E + PH are concerned with postmenopausal women and the effects of relatively short periods of treatment, it is concluded that the relationship of exogenous E to cancer in younger women taking E + PH contraceptives has not yet been determined. The current state of knowledge concerning this relationship is compared to the state of knowledge concerning the relationship between smoking and lung cancer, prior to the demonstration of this significant statistical relationship by extensive epidemiologic studies.

- 70-3 MECHANISMS OF ACTION OF CARCINOGENIC AROMATIC AMIDES. (E.) Gutmann, H. R. (U. Minnesota, Minneapolis), E. J. Barry and D. Malejka-Giganti. J. Nat. Cancer Inst. 43(1): 287-291, 1969. (16 references)

Data suggesting that metabolic activation of aromatic amides may be accomplished by N-hydroxylation and transformation to a reactive amidonium ion (which combines with tissue protein and/or nucleic acids) are discussed. Evidence is presented to suggest the participation of 2-fluorenyl-hydroxylamine in the formation of protein adducts in the rat liver, after admin. of N-2-fluorenylacetamide.

- 70-4 STUDIES ON THE NATURE OF THE PROXIMAL BLADDER CARCINOGENS. (E.) Troll, W. (New York U. Med. Ctr., New York), S. Belman and F. Mukai. J. Nat. Cancer Inst. 43(1):283-286, 1969. (15 references)

It is suggested that the proximal bladder carcinogens of β -naphthylamine in dogs and man are the phosphate esters, bis(2-amino)-1-(naphthyl)

phosphate and its N-hydroxylated form (slightly ether-soluble and ether-soluble, resp.).

- 70-5 CARCINOGENIC METABOLITES OF TRYPTOPHAN. (Rus.) Zasyanka, A. T. (N. N. Petrov Res. Inst. Oncol., Leningrad, USSR). Vop. Onkol. 15(7):108-118, 1969. (31 references)

Bladder carcinogenesis by tryptophan metabolites in animals and man is discussed. Most of the references are from papers published in English.

- 70-6 OCCUPATIONAL CANCERS. (Por.) Pereira, M. F. Hospital (Rio) 75(3): 885-895, 1969. (11 references)

After a discussion of several current theories of carcinogenesis, the commonest occupational carcinogens (including radiation) and their effects are reviewed.

- 70-7 HOW VALUABLE THE DOG IN THE ROUTINE TESTING OF SUSPECTED CARCINOGENS? (E.) Bonser, G. M. (U. Leeds Algernon Firth Inst. Path., England). J. Nat. Cancer Inst. 43(1):271-274, 1969. (21 references)

Long-term carcinogen testing in the dog is reviewed, with reference to the best use of facilities, finances and personnel. It is concluded that, except in special cases, routine experiments should be performed in rodents rather than in dogs.

- 70-8 ONCOGENES OF RNA TUMOR VIRUSES AS DETERMINANTS OF CANCER. (E.) Huebner, R. J. (NCI, Bethesda, Md.) and G. J. Todaro. Proc. Nat. Acad. Sci. USA 64(3):1087-1094, 1969. (75 references)

Evidence for the existence of information for producing C-type RNA viruses in the cells of many (perhaps all) vertebrates is presented. It is postulated that the viral information (virogene), including that portion responsible for neoplastic transformation of a normal cell (oncogene), is most commonly transmitted in a covert form from an animal or a cell to its progeny. Partial or complete activation of these genes is favored by irradiation, carcinogens and the aging process.

- 70-9 HERPESVIRUSES AND CANCER. (E.) Goodheart, C. R. (535 N. Dearborn St., Chicago, Ill.). JAMA 211(1):91-96, 1970. (14 references)

The properties of 6 definitely or possibly oncogenic herpesviruses of non-human vertebrates

(causing Lucké renal tumor of frogs, Marek's disease of chickens, a rabbit lymphoma, a monkey lymphoma, and possibly a leukemia and "wet tail" in guinea pigs), and the possible relationships of 2 human herpesviruses to human cancer (Epstein-Barr virus in Burkitt's lymphoma; genital Type 2 infections in carcinoma of the cervix), are discussed.

- 70-10 CELL TRANSFORMATION BY VIRUSES. (E.) Dulbecco, R. (Salk Inst. Biol. Studies, San Diego, Calif.). Science 166(3908):962-968, 1969. (54 references)

Mechanisms of virus-induced transformation are discussed, with particular reference to changes observed in cells exposed to SV40 and polyoma virus.

- 70-11 THE CELL SURFACE IN IMMUNE RESPONSE. (E.) Klein, E. (Karolinska Inst., Stockholm). Europ. J. Cancer 6(1):15-22, 1970. (59 references)

The properties of tumor-specific transplantation antigens in experimental tumors (induced by chemicals and viruses), evidence supporting the existence of such surface antigens in human tumors (especially Burkitt's lymphoma and cancer of the nasopharynx, related to a herpes-type virus), and the phenomenon of immunological enhancement, are discussed.

- 70-12 THE CANCER CELL AS A STEM CELL UNABLE TO DIFFERENTIATE. A THEORY OF CARCINOGENESIS. (E.) Fiala, S. (U. Southern California, Los Angeles). Neoplasma (Bratisl.) 15(6):607-622, 1968. (89 references)

Evidence is presented to support the hypothesis that carcinogens, by inhibiting adaptive formation of the system of cytoplasmic structures in response to tropic hormonal influences from the organism, prevent the differentiation of the stem cells. The differentiation depends on a synchrony between intracellular-nuclear and cytoplasmic genetic systems. Dissynchronization results if the cell is removed from the organism (thereby removing it from the supply of necessary tropic hormonal influences) or exposed to carcinogenic influences. This pattern of synchrony or dissynchronization is probably related to methylation of the nucleic acids. In the malignant cells, the genetic information is complete, but present in functional disarray.

- 70-13 NEW APPROACH TO CANCER. (E.) Burch, P. R. J. (U. Leeds Gen. Infirm., England). Nature (London) 225(5233):512-516, 1970. (41 references)

It is suggested that normal growth, beyond a certain stage of embryogenesis, is regulated by

a central mesenchymal system by a homeostatic or feedback mechanism. A breakdown of the central portion of this control system (the 2 principal parts of which correspond to the anatomical division of target tissues on each side of the blood-tissue barrier) results in the development of many age-related neoplastic and non-neoplastic diseases. Evidence is presented to suggest that the development of malignant tumors begins with initiating somatic mutations in the central (mesenchymal) growth-control stem cells, not in the cells of the target tissue which later becomes neoplastic.

- 70-14 PLASMA CELL NEOPLASMS OF MAN AND ANIMALS. (E.) Lingeman, C. H. (NCI, Bethesda, Md.). Nat. Cancer Inst. Monogr. 32:303-311, 1969. (63 references)

This paper includes a brief discussion of the epidemiology of multiple myeloma in several nations.

- 70-15 SKIN, HEREDITY, AND CANCER. (E.) Lynch, H. T. (Creighton U. Sch. Med., Omaha, Neb.). Cancer 24(2):277-288, 1969. (114 references)

Hereditary skin cancers, and other hereditary skin lesions which may predispose to skin cancer or be associated with cancer at other locations, are discussed.

- 70-16 THE IMMUNOLOGIC CAPABILITY OF PATIENTS WITH LYMPHOMA. (E.) Miller, D. G. (Cornell U. Med. Coll., New York, N. Y.). Cancer Res. 28(7):1441-1448, 1968. (49 references)

Infectious diseases, autoimmune complications and second primary tumors as complications of leukemia and lymphoma are discussed. It is suggested that pts. with lymphoproliferative diseases have a defective immunological defense against environmental and possibly endogenous pathogens (microbial pathogens, allergens and carcinogens). A hypothetical relationship between the pathogenesis of Hodgkin's disease and thymus-dependent lymphocytes, and the pathogenesis of chronic lymphocytic leukemia in relation to non-thymus-dependent lymphocytes, is presented.

- 70-17 Experimentelle Geschwülste Des Zentralnervensystems - Induktion, Morphologie, Transplantation und Anwendung. (Experimental Tumors of the Central Nervous System - Induction, Morphology, Transplantation and Development.). (Ger.) Jänisch, W. and D. Schreiber. VEB Gustav Fischer Verlag, 1969, 180 pp.

70-18 STATISTICAL STUDY ON THERAPEUTIC IRRADIATION AND LEUKAEMOGENESIS IN MAN. (Jap.) Kitabatake, T. (Niigata U. Sch. Med., Japan). Acta Haemat. (Jap.) 31(5):805-809, 1968.

Of 1197 pts. with leukemia and 2609 controls (seen in 1961-1965 at several large hospitals in Japan), 5.6% and 6.1% (68 and 159 pts.), resp., had histories of medical irradiation, X-ray fluoroscopy or radiotherapy (RT). This difference was not statistically significant; however, the pts. with leukemia showed significantly higher frequencies of RT and high doses of fluoroscopic radiation (1.59% and 2.51%, resp.) than the control group (0.50% and 0.65%, resp.). In 1953-1965, 10 pts. developed leukemia after postoperative RT for breast cancer in Japan, compared to 8 expected cases (118,000 person-yr. at risk); this difference was significant at the 1% level. In the 49 previously reported cases of RT-induced leukemia in Japan, the distribution of the disease types was similar to that seen for all leukemias in Japan, but a difference in age distribution was found. As with other radiation-induced tumors, the latent periods for these radiation-induced leukemias were distributed in a nearly log-normal curve. A slight tendency towards an association between a high radiation dose and a short latent period was noted, but no correlation was seen between the duration of the latent period and the age at irradiation.

70-19 ETIOLOGIC ROLE OF IONIZING RADIATION ON THE DEVELOPMENT OF LEUKEMIA: CLINICAL AND STATISTICAL STUDIES ON LEUKEMIA IN PATIENTS TREATED WITH RADIOIODINE AND IN ATOMIC BOMB SURVIVORS. (Jap.) Hoshino, T. (Kyoto U., Japan). Acta Haemat. (Jap.) 31(5):825-831, 1968.

Among pts. admin. ^{131}I for thyrotoxicosis in Japan, the observed number of cases of leukemia (2 cases) at the end of 1965 was not significantly higher than the expected number of cases (0.4/18,513 person-yr. of radiation exposure). In the 42 reported cases of ^{131}I -induced leukemia, the acute:chronic leukemia ratio was higher (as was the frequency of aleukemia) than in leukemic pts. without histories of radiation exposure. The leukemogenic radiations from ^{131}I were apparently the β - and γ -rays. At the end of 1967, 407 leukemias had been found among the radiation-exposed populations of Hiroshima (169 acute, 85 chronic leukemias) and Nagasaki (125 acute, 28 chronic leukemias); in both cities, the peak occurrence was seen in 1950-1953. In Hiroshima and Nagasaki, the av. annual leukemia incidence/ 10^5 population increased with radiation doses above 20 and 100 rads, resp. Differences between the 2 cities in the radiation dose-effect relationship and the types of leukemia observed, are discussed in terms of the relationship between the acute:chronic leukemia ratio and the γ /neutron ratio of the radiation dose.

In pts. developing leukemia after either atomic radiation exposure or ^{131}I therapy for thyrotoxicosis, the initial biological effects of the radiation (hyperthyroidism with ^{131}I , cataracts after atomic exposure, leukopenia in both groups) were significantly more severe than in similarly exposed persons who did not develop leukemia.

70-20 SYNERGISTIC ACTION OF RADIATION AND VIRUS IN INDUCTION OF LEUKEMIA IN RATS. (E.) Yokoro, K. (Hiroshima U. Res. Inst. Nuclear Med., Japan), T. Ito, N. Imamura, A. Kawase and T. Yamasaki. Cancer Res. 29(11):1973-1976, 1969.

In Wistar/Furth (W/Fu) rats inj. neonatally with Gross leukemia virus (GLV), typical thymic lymphomas developed in 100% of the animals after latent periods of 80-90 days. This susceptibility decreased rapidly with age; W/Fu rats inj. with GLV at age 7-8 wk. developed no leukemias. In 4-5-wk.-old W/Fu rats, total-body irradiation (TBR; 600 r) did not induce leukemias, although 2/5 females developed mammary tumors 9-12 mo. after TBR. In W/Fu rats treated with both TBR and GLV (at ages 4-5 and 7-8 wk., resp.), leukemias developed in 5/8 males (62.5%) and 6/12 females (50%) after 77-213 days. Latent periods for the thymic lymphomas (seen in 7/13) were shorter than the latent periods for the other leukemias. Cell-free filtrates from 2 thymic lymphomas showed persistent GLV activity, as demonstrated by their ability to induce leukemia in neonatal W/Fu rats. It is suggested that TBR promoted an interaction between the target cell and GLV and a proliferation of antigenically altered leukemic cells.

70-21 POSTPONEMENT OF MURINE RADIOGENIC LEUKEMIA BY MANIPULATION OF THE PRE-LEUKEMIC STATE. (E.) Ludwig, F. C. (U. California Sch. Med., San Francisco), R. M. Elashoff and O. N. Rambo. Proc. Soc. Exp. Biol. Med. 130(4):1285-1288, 1969.

In RFM/U mice treated with leukemogenic doses of total-body irradiation (TBR; 350 rads) at age 60-90 days, admin. of the same dose of TBR during the preleukemic stage (70 days after the first TBR) delayed the development of leukemia and significantly increased the av. survival time. Admin. of 6-mercaptopurine (25 mg/kg/day x 10 days) during the preleukemic stage retarded the development of leukemia, but did not affect the av. survival times (evaluated in mice surviving 425 days or more). Only in the last stages of the life span did the 3 groups of mice show the same probability of death from leukemia. It is concluded that the preleukemic stage (between recovery from acute radiation injury and the development of overt malignancy) is

radiosensitive and involves changes other than simple immunosuppression.

- 70-22 AN ELEMENTARY THEORY LEADING TO NON-LINEAR DOSE-RISK RELATIONSHIPS FOR RADIATION CARCINOGENESIS. (E.) Wright, J. K. (Berkeley Nuclear Labs., Gloucestershire, England) and R. Peto. Brit. J. Cancer 23(3):547-553, 1969.

Mathematical models are developed for a 2-stage theory of radiation carcinogenesis, in which the inhibition of carcinogenesis breaks down if a small number of radiation-activated cells lie close enough together that they can interact in some way. Another model is considered, which assumes that tumor growth is resisted by a diffusing inhibiting substance (which is absorbed and must be maintained at a certain critical level throughout the body in order to inhibit tumor development). Assuming the existence of a closely grouped cluster of activated cells, a non-linear dose-risk relationship is demonstrated. In the system including the diffusing inhibiting substance, a power dose-risk relationship was demonstrated.

- 70-23 BREAST NEOPLASMS IN WOMEN TREATED WITH X-RAYS FOR ACUTE POSTPARTUM MASTITIS. A PILOT STUDY. (E.) Mettler, F. A., Jr. (Jefferson Med. Coll., Philadelphia, Pa.), L. H. Hempelmann, A. M. Dutton, J. W. Pifer, E. T. Toyooka and W. R. Ames. J. Nat. Cancer Inst. 43(4):803-811, 1969.

The breast tumor incidence after radiotherapy (RT) for acute postpartum mastitis was studied in 606 women. The mean follow-up period after RT was 18.25 yr. (10-25 yr. in most cases). The expected numbers of malignant breast tumors in 1962 and 1967 (based on 1958-1960 data for upstate New York) were 3.06 and 5.86, resp.; the observed numbers were 5 and 13, resp. This significant excess of malignant breast tumors was closely related to the site(s) of prior RT for mastitis. The treated women also showed a total of 25 benign breast tumors (21 pts.); the expected number of cases was 4-5. The association between the site(s) of prior RT and the site(s) of tumor development was not as strong for the benign breast tumors as for the malignant breast tumors. No good correlation between the RT dose and the incidence of benign or malignant breast tumors was found. These women also showed 2 leukemias and 1 case each of Hodgkin's disease and multiple myeloma, a significant excess over the 1.13 expected neoplasms of the blood-forming organs. Radiation exposure itself could not be implicated as an etiologic factor in neoplastic transformation on the basis of this study (which lacked adequate controls); however, it is concluded that at least some of the breast cancers in this group could have been induced by prior exposure to X-rays.

- 70-24 MALIGNANT PHAGEDENIC ULCERS OF THE LEG. CRITICAL REVIEW OF 235 CASES SEEN IN DAKAR BETWEEN 1959 AND 1964. (Fr.) Serafino, X. and P. A. Menye. Bull. Cancer (Paris) 55(3): 353-398, 1968.

On the basis of data obtained from these 235 pts. with phagedenic ulcers of the lower legs (predominantly over the tibia) undergoing malignant transformation, it is estimated that carcinomas will develop in about 10-15% of phagedenic ulcers. The pts. seen in 1960-1964 were predominantly young adults (usually 30-35 yr. old; 114 women, 88 men). Nearly all pts. came from rural areas and 90% had worked in farming or stock raising. The tumors arose in old, neglected, repeatedly traumatized ulcers. Superinfections, vascular occlusion and/or vasospasm were present in most cases. All phagedenic ulcers were sclerohyperplastic, with multiple foci of spinocellular carcinoma. Inguino-crural lymphadenopathy was present in 85% of the pts., but only 30% showed lymph node invasion by tumor cells. Except for the relatively short latent period (usually about 5 yr. from the onset of the ulcer to the diagnosis of carcinoma), these tumors in phagedenic ulcers were similar to those developing in fistulas or on burn scars.

- 70-25 RADIATION-INDUCED SKIN CANCER OF THE HEAD AND NECK. (E.) Martin, H. (Mem. Hosp. Cancer Allied Dis., New York, N. Y.), E. Strong and R. H. Spiro. Cancer 25(1):61-71, 1970.

In 368 pts. with skin tumors (predominantly basal cell and squamous cell carcinomas) which developed after radiotherapy (RT) for benign skin conditions of the head and neck (acne or hirsutism in 62% of the evaluable pts.), the female:male ratio was about 3:1. The age at the time of RT was 1-73 yr. (median 23 yr.); the age at the diagnosis of cancer was 19-89 yr. (median 49 yr.). Latent periods were 1-64 yr. (median 21 yr.) in 357 evaluable pts. Latent periods were 3-10 yr. in 4/7 pts. developing cancer before age 26 yr. A causative relationship was apparent in 3 young pts. who developed skin cancer 3-5 yr. after RT, but the significance of the 1-2-yr. latent periods reported for 4 pts. was considered questionable. Since the latent period was 31-50 yr. in 73 pts. (about 20%) and 40 yr. or more in 22 pts., it is concluded that the risk of tumor development in irradiated skin persists throughout life. An unusually high proportion of these pts. developed regional and distant tumor spread; 35 pts. died of uncontrolled RT-induced skin carcinoma.

- 70-26 INDUCTION OF HEMATOPOIETIC NEOPLASMS IN MINIATURE SWINE BY CHRONIC FEEDING OF STRONTIUM-90. (E.) Howard, E. B. (Battelle Mem. Inst., Richland, Wash.) and W. J. Clarke. J. Nat. Cancer Inst. 44(1):21-38, 1970.

Effects of chronic ^{90}Sr feeding (1-3100 $\mu\text{C}/\text{day}$ throughout life) were studied in 750 miniature swine (Pltman-Moore strain; parental, F_1 and F_2 generations). Myeloid metaplasia, lymphomas, myeloid neoplasms (usually acute or chronic granulocytic leukemia) and stem cell neoplasms (undifferentiated leukemia type) developed in 29/224, 17/224, 20/224 and 3/224 treated animals at risk, resp. Bone sarcomas also developed in 7/224, always secondary to leukoproliferative disorders. The only neoplasms seen in 146 untreated controls were 2 cases of chronic granulocytic leukemia. The higher tumor incidence and shorter latent periods noted in the F_1 and F_2 generations indicated the importance of radiation exposure in utero and through colostrum; 16/17 of the lymphoid neoplasms were seen in animals of the F_1 and F_2 generations. It is concluded that doses of ^{90}Sr which result in uniform skeletal deposition affect the hematopoietic tissue much more than the bone.

70-27 TUMOR-INDUCING EFFECT OF X-RAYS IN Drosophila AFTER PARTIAL IRRADIATION OF NON-SEGMENTED EGGS. (Fr.) Ghelelovitch, S. (Inst. Radium Pasteur Lab., Paris). Int. J. Radiat. Biol. 16(1):15-26, 1969.

70-28 INFLUENCE OF X-IRRADIATION AND THE MILK AGENT ON GROWTH OF TRANSPLANTED MOUSE MAMMARY TUMORS. (E.) Prehn, R. T. (U. Pennsylvania Sch. Med. Inst. Cancer Res., Philadelphia). J. Nat. Cancer Inst. 43(6): 1215-1220, 1969.

70-29 DNA REPLICATION IN RADIATION-INDUCED THYMOMAS OF C57BL MICE. (E.) Lagerlöf, B. (Karolinska Inst., Stockholm) and H. Takahashi. Acta Cytol. (Balt.) 14(1):6-10, 1970.

70-30 METASTASIZING THYROID CANCER TEN YEARS AFTER RADIOACTIVE IODINE TREATMENT FOR HYPERTHYROIDISM. (E.) Stamler, F. W. (U. Iowa Coll. Med., Iowa City), R. D. Liechty and E. L. DeGowin. J. Iowa Med. Soc. 60(1):16-20, 1970.

70-31 BIOASSAY OF PESTICIDES AND INDUSTRIAL CHEMICALS FOR TUMORIGENICITY IN MICE: A PRELIMINARY NOTE. (E.) Innes, J. R. M., B. M. Ulland, M. G. Valerio, L. Petrucelli, L. Fishbein, E. R. Hart, A. J. Pallotta, R. R. Bates (NCI, Bethesda, Md.), H. L. Falk, J. J. Gart, M. Klein, I. Mitchell and J. Peters. J. Nat. Cancer Inst. 42(6):1101-1114, 1969.

Male and female (C57BL/6 x C3H/Anf) F₁ and (C57BL/6 x AKR)F₁ mice were treated with a series of 120 pesticides and industrial chemicals (72 mice received each test compound), by gavage from age 1-4 wk., and then mixed with food until sacrifice at age 18 mo. A significant increase in tumor incidence (principally hepatomas, but also lymphomas and lung tumors) was seen with 5 insecticides, 1 herbicide and 5 fungicides: pentachloronitrobenzene (PCNB; 464 mg/kg/day), 2,2-bis(p-chlorophenyl)-1,1,1-trichloroethane (p,p'-DDT; 46.4 mg/kg/day), dodecachlorooctahydro-1,3,4-metheno-2H-cyclobuta[cd]-pentalene (Mirex; 10 mg/kg/day), 2,3-dichloroallyl diisopropyl thiocarbamate (Avadex; 215 mg/kg/day), bis(2-chloroethyl)ether (100 mg/kg/day), selenium diethyldithiocarbamate (ethyl selenac; 10 mg/kg/day), ethylene thiourea (ETU; 215 mg/kg/day), N-(2-hydroxyethyl)-hydrazine (2.15 mg/kg/day), ethyl 4,4'-dichlorobenzilate (chlorobenzilate; 215 mg/kg/day), bis(2-hydroxyethyl)dithiocarbamic acid potassium salt (464 mg/kg/day) and terpene polychlorinates (Strobane; 4.64 mg/kg/day). No significant carcinogenic effects were seen with 89 compounds; 20 compounds are under further investigation.

70-32 CONTAMINATING ORGANIC MATERIAL IN ASBESTOS. (E.) Commins, B. T. (St. Bartholomew's Hosp. Med. Coll., London) and G. W. Gibbs. Brit. J. Cancer 23(2):358-362, 1969.

Canadian chrysotile stored in polyethylene bags absorbed oil from the polyethylene, and converted a constituent of this oil to diphenoquinone. The organic material extracted from asbestos was weakly carcinogenic in rats, but the carcinogenic properties of the oxidation products of polyethylene were unknown.

70-33 BLASTOMITOTIC AGENTS IN LEGUMINOSAE AND OTHER FAMILIES. (E.) Parker, J. W. (U. Southern California Sch. Med., Los Angeles), J. Steiner, A. Coffin, R. J. Lukes, K. Burr and L. Brilliantine. Experientia 25(2): 187-188, 1969.

Lymphocyte cultures from healthy donors, prepared by gelatin sedimentation of defibrinated blood, were exposed to seed extracts from several plants in culture tubes (0.01 or 0.1 ml). The reference for mitogenicity was an extract of red kidney beans (Phaseolus vulgaris). Significant

cell transformation at 72 hr. was seen with extracts from P. vulgaris (49.6-65.8%), Datura discolor (42.8%), Trixis californica (38.6%), Ephedra nevadensis (2.5%) and Mammea safra (19.4%). The blast cells appearing after addition of the extracts were indistinguishable from those formed in phytohemagglutinin-exposed cultures.

70-34 UPTAKE OF RADIOACTIVE LABELED CARCINOGEN BY THE ORAL MUCOUS MEMBRANE. (Ger.) Schilli, W., W. Hamann and W. Oehlert. Fortschr. Kiefer. Gesichtschir. 13:228-231, 1968.

No difference between the regeneration mode of cells from the oral mucous membrane (tongue, cheek and cheek pouch) and cells from the skin of the back was noted 1, 48 and 96 hr. after i.p. inj. of ³H-labeled thymidine in adult Syrian golden hamsters. Spray applications of ³H-labeled 3,4-benzpyrene (0.2 mg) produced necrotic areas in the cheek pouch, but penetrated only into the superficial layers of the mucosa of the tongue and oral cavity (in contrast to its deep penetration into the skin).

70-35 A STUDY OF TOBACCO CARCINOGENESIS. X. TUMOR PROMOTING ACTIVITY. (E.) Wynder, E. L. (Sloan-Kettering Inst. Cancer Res., New York, N. Y.) and D. Hoffmann. Cancer 24(2):289-301, 1969.

Female Swiss albino mice were admin., initiating doses of 7,12-dimethylbenzanthracene (DMBA; 150 or 300 µg x 1, topically) at age 7-8 wk.; applications of tobacco tars (av. dose 75 mg; 3 paintings/wk. x 12 mo.) were begun 10 days after DMBA admin. With the higher initiating dose of DMBA, the latent period was shorter than with the lower dose, and a greater number of tumors appeared earlier; however, the final tumor yield was comparable for both doses. In animals initiated with DMBA (as above), the tumor-promoting activity of preparations from cigarettes made from tobacco stems was significantly lower than the activity of cigarette tobacco from cuts (standard). No significant difference between the number of tumor-bearing mice was seen with tars from cigarettes containing additive (8.3% sodium nitrate or 5% copper) and control cigarettes. In mice treated with DMBA and tar from hay cigarettes, tumors appeared later and were fewer than after admin. with cigarette smoke. The tumor-promoting activity of spinach tar was similar to that of tobacco tar. Tumor-promoting activities of Turkish tobacco and standard cigarette smoke condensate were similar.

70-36 PROTECTION OF CULTURED HAMSTER EMBRYONIC CELLS FROM 7,12-DIMETHYLBENZ

(a) ANTHRACENE CYTOTOXICITY AND THE INDUCED SYNTHESIS OF ARYL HYDROXYLASE. (E.) Alfred, L. J. (Catholic U., Washington, D. C.), P. J. Donovan, M. S. Baker and J. A. DiPaolo. Cancer Res. 29(10):1805-1809, 1969.

DNA synthesis in secondary cultures of Syrian hamster embryonic tissue was blocked with excess thymidine (TdR). After release, an early and rapid incorporation of ^3H -labeled cytidine (CdR) into DNA was noted; CdR incorporation reached a max. rate about 1 hr. before the beginning of incorporation of ^{14}C -TdR. Addition of exogenous ^3H -CdR restored the normal rate of DNA synthesis. Addition of 7,12-dimethylbenzanthracene (DMBA) had only a slight effect on ^3H -CdR incorporation, but significantly reduced ^{14}C -TdR incorporation during DNA synthesis. Exposure to an equimolar conc. of benzanthrane (BA; 4 μM) protected the cells from DMBA toxicity, ostensibly by induction of aryl hydroxylase, which may have degraded the DMBA to nontoxic metabolites. The enzyme-inducing effect of BA + DMBA was greater than the effect of either agent alone. The high rate of enzyme formation during thymidine-inhibited DNA synthesis suggested that cells in the G₁-S phase of the mitotic cycle synthesized this enzyme system as efficiently as cells in progress through other phases of the cell cycle.

70-37 ON THE DNA AND HISTONE CONTENT OF N-NITROSOMETHYLUREA INDUCED RAT TUMOURS. (E.) Jobst, K. (Univ. Med. Sch., Inst. Path., Pécs, Hungary). Neoplasma (Bratisl.) 16(1): 43-51, 1969.

Cytophotometric studies were made of tumors induced in home-bred albino rats by inj. of N-nitrosomethylurea (NMU); syringoadenomas (total dosage, 17.5 mg i.p.); bronchial papillomas and renal sarcomas (38.5 mg i.v.); adenomas and carcinomas of the thyroid (17.5 mg i.p.); oligodendrogliomas (38.5 mg i.v.); and leukemic infiltration of the liver (17.2 mg i.v.). On the basis of DNA and histone protein content, 2 types of NMU-induced tumors were seen: those in which the DNA and protein contents were similar to that of normal tissue (syringoadenomas, thyroid adenomas, bronchial papillomas, leukemia) and tumors with DNA and histone contents 40-80% above control values (renal sarcomas, oligodendrogliomas, thyroid carcinomas). The results suggest the presence of euploid and aneuploid sets of chromosomes in the tumors studied.

70-38 INDUCTION OF SARCOMAS IN RATS BY SOLID AND FRAGMENTED POLYETHYLENE: EXPERIMENTAL OBSERVATIONS AND CLINICAL IMPLICATIONS. (E.) Carter, R. L. (Roy. Cancer Hosp., Chester Beatty Res. Inst., London) and F. J. C. Roe. Brit. J. Cancer 23(2):401-407, 1969.

Local tumors developed in 7/20 male CB stock rats (8 wk. old at the beginning of the experiment)

Implanted s.c. with a single polyethylene segment (approx. 620 mg); the tumors developed 48-79 wk., (mean 52 wk.) after implantation. After implantation of shredded plastic packed into gelatin capsules, 5/20 rats developed s.c. sarcomas after 41-77 wk. (mean 60 wk.) No tumors developed in 20 sham-operated animals or in 20 animals implanted with empty gelatin capsules.

70-39 EARLY DEVELOPMENT OF INJECTION-SITE SARCOMAS IN RATS: A STUDY OF TUMOURS INDUCED BY A RUBBER ADDITIVE. (E.) Carter, R. L. (Roy. Cancer Hosp., Chester Beatty Res. Inst., London). Brit. J. Cancer 23(2):408-416, 1969.

In Sprague-Dawley rats inj. s.c. or i.p. at age 7-8 wk. with polymerized N-nitroso-2,2,4-trimethyl-1,2-dihydroquinoline (NTDQ; 1 inj./wk. of 25 mg x 20 in alternating flanks) in polyethylene glycol (0.25 ml.), a large proportion of the inj. site sarcomas observed (16/20 in males, 8/20 in females admin. NTDQ s.c.; 2/20 males and 1/20 in females inj. i.p.) were unsuspected during life, and were diagnosed at autopsy or by histological examination, 96-106 wk. after inj. Only 4/20 males and 1/20 of the females admin. NTDQ s.c. developed sarcomas during life (81-106 wk.) and 1/20 males developed a sarcoma after i.p. inj. No sarcomas were observed in animals force-fed NTDQ (3 doses/wk. of 25 mg x 20 wk.) or in rats admin. propylene glycol (1 inj./wk. of 0.25 ml s.c. in alternating flanks x 20 wk.), but 1 untreated control developed a sarcoma of the chest wall. In animals force-fed NTDQ, 1/20 males and 1/20 females developed fibromas.

70-40 THE FINE STRUCTURE OF METHYLCHOLANTHRENE-INDUCED TUMORS IN MICE. (E.) Clarke, M. A. (U. Washington Sch. Med., Seattle). Cancer 24(1):147-157, 1969.

Implants (s.c.) of a 3-methylcholanthrene (0.1 mg)-impregnated discs, into the flanks of C3H, C57BL and Balb/C mice, induced palpable fibrosarcomas or rhabdomyosarcomas (10-15 mm in diameter) within 3-6 mo. The primary tumors, tumors of the first transplant generation and tumor cells in vitro were ultrastructurally similar, containing rhabdomyoblasts in various degrees of differentiation. Striated myofilaments were seen in bundles within the rhabdomyoblasts. One transplanted tumor contained myofilaments, but the cells in culture did not; however, some cells contained myofilaments that were seen under the electron microscope, but not the light microscope. Extracellular virus-like particles (VLP) were seen in cell cultures of tumors from all strains of mice. The distribution and frequency of these VLP were not related to tumor type or the strain of origin. No evidence of intracellular multiplication of the VLP was

noted in any of the preparations examined. VLP were rare in the in vivo tumors. The significance of these VLP could not be determined.

70-41 SARCOMA INDUCTION IN MICE BY METHYLCHOLANTHRENE. THE INFLUENCE OF THYMUS GRAFTING AND OF CASTRATION. (E.) Marchant, J. (Med. Sch. Cancer Res. Labs., Birmingham, England). Brit. J. Cancer 23(2):377-382, 1969.

Male and female (C57BL x IF)_{F1} mice received s.c. thymus grafts from syngeneic animals of the same sex (6-10 days old) at 2-wk. intervals from age 2 mo.; 3-methylcholanthrene (MC; 1.0 mg s.c. in olive oil) was admin. 5 wk. after the initial graft. Another group of non-grafted mice underwent oophorectomy (oox.) or orchiectomy (orx.) at age 2 mo., and received MC (as above) 5 wk. later. No difference in tumor incidence was seen between thymus-grafted animals and non-grafted controls. All males developed sarcomas at the inj. site within 20 wk. The females were relatively resistant to sarcoma development, but developed leukemia and mammary adenocarcinomas. All oox. or orx. animals developed sarcomas at the inj. site, but no other tumors were seen. Mean latent periods were 17.0 wk. in orx. males and 19.1 wk. in oox. females.

70-42 SARCOMA INDUCTION IN MICE BY METHYLCHOLANTHRENE. ANTIGENICITY TESTS OF SARCOMAS INDUCED IN THYMUS GRAFTED AND CONTROL ANIMALS. (E.) Marchant, J. (Med. Sch. Cancer Res. Labs., Birmingham, England). Brit. J. Cancer 23(2):383-390, 1969.

Male and female (C57BL x IF)_{F1} mice were admin. 3-methylcholanthrene (MC; 1 mg s.c. in olive oil) at age 3 mo.; 12/24 also received a s.c. graft of whole syngeneic thymus gland (1 graft every 2 wk.), beginning 5 wk. before MC inj. Sarcomas developed in 22/24 mice, 12.5-19 wk. after MC inj. Sarcomas from thymus-grafted animals were not less antigenic than those from controls.

70-43 THE ROLE OF THE REGIONAL LYMPH NODES IN THE IMMUNITY TO A CHEMICALLY INDUCED SARCOMA IN C3H MICE. (E.) Bard, D. S. (Boston Hosp. Women, Mass.), W. G. Hammond and Y. H. Pilch. Cancer Res. 29(7):1379-1384, 1969.

The physiological function of regional lymph nodes was studied in 10-14-wk.-old inbred C3H/HeN female mice bearing second- and third-generation 3-methylcholanthrene-induced sarcomas. No alteration of cumulative mortality, tumor incidence or mean tumor vol. was seen in unilaterally lymphadenectomized mice inoc. with tumor either distal to the lymph node removal or in the contralateral hindlimb. Regional lymphadenectomy had no effect on the growth of previously established tumor, or on the immune response to a subsequent challenge with the same

tumor. Inj. (i.p.) of lymph node cells from tumor-bearing mice produced adoptive immunity in isologous hosts.

70-44 TUMORS DEVELOPING IN OOPHORECTOMIZED SPRAGUE-DAWLEY RATS AFTER A SINGLE GASTRIC INSTILLATION OF 7,12-DIMETHYLBENZ(a)ANTHRACENE. (E.) Heimann, R. (Free U. Brussels, Belgium), J. C. Heuson and A. Coune. Cancer Res. 28(2):309-313, 1968.

Female Sprague-Dawley rats, oophorectomized at age 46 days, were admin. a single dose of 7,12-dimethylbenzanthracene (20 mg p.o. in sesame oil) 7 days later; 11/64 died between 7-9 mo. and the rest were sacrificed after 12 mo. Mammary tumors were seen in 12 rats; 1 mammary carcinoma developed in each of 3 rats which died early, and 9 rats developed a total of 10 fibroadenomas. Tumors of Zymbal's gland (ear duct) were seen in 38 (59%; unilateral in 36%, bilateral in 23%), becoming externally visible by 5 mo. Only about 20% of these tumors were carcinomas; some were pseudosarcomas and the rest were adenomas. A total of 17 skin lesions developed in 14 rats (22%), consisting of 6 epidermal cysts, 4 keratoacanthomas, 2 sebaceous epitheliomas, 2 basal cell epitheliomas, 1 warty papilloma, 1 sebaceous cyst and 1 trichoepithelioma. Neurofibrosarcomas developed on the ears in 41 rats (64%; bilateral tumors were seen in 11, or 17%). Other tumors included 2 leukemias, 2 low-grade dermal fibrosarcomas of the neck and 1 retroperitoneal fibrosarcoma.

70-45 "SEBACEOUS GLANDS" AND "HYPERPLASIA" TESTS AS SCREENING METHODS FOR TOBACCO TAR CARCINOGENESIS. (E.) Chouroulinkov, I. (Cancer Res. Inst., Villejuif, France), P. Lazar, C. Izard, C. Libermann and M. Guérin. J. Nat. Cancer Inst. 42(6):981-985, 1969.

Albino IC mice (52 days old) received 3 topical applications of smoke condensates (0.05 ml of 30%, 45% or 60% condensate in methanol) from cigarettes made with tobacco leaf ribs (R) or parenchyma (P), with or without added humectant (H). The treated area was removed 8 days later. Sebaceous gland tests showed increasing activity with H+R, R, H+P and P, resp. In long-term tests, each mouse received an initial application 7,12-dimethylbenzanthracene (150 µg in methanol); application of the condensates (as above) was begun 3 wk. later and continued (3 doses/wk.) until death. The first tumors appeared at 45 wk. The percentage of tumors was correlated with the short-term results; the incidence increased from H+R, R, H+P to P, resp.

70-46 INHIBITION BY ACTINOMYCIN D OF DNA SYNTHESIS AND SKIN TUMORIGENESIS INDUCED BY 7,12-DIMETHYLBENZ(a)ANTHRACENE. (E.) Bates, R. R. (NIH, Bethesda, Md.), J. S. Wortham,

W. B. Counts, C. W. Dingman and H. V. Gelboin. Cancer Res. 28(1):27-34, 1968.

DNA synthesis in the skin of random-bred male NIH General Purpose Swiss mice was inhibited by topically applied actinomycin D (AD; 24-60 μ g) at doses similar to those required to inhibit skin carcinogenesis by topical application of 7,12-dimethylbenzanthracene (DMBA; 16 μ g). Tumorigenesis was inhibited 76-92% at AD doses of 50-90 μ g, 26-79% at 20-40 μ g, and 31-63% with 15 μ g (the latter in 1/3 trials). On the basis of the similarity of the anti-tumorigenic and anti-DNA synthesis doses of AD, it is suggested that either DNA synthesis or a process associated with cell replication is necessary for the initiation of DMBA-induced skin tumors.

70-47 CARCINOGENESIS AND INHIBITED BIO-SYNTHESIS OF SOLUBLE MOUSE SKIN PROTEINS BY ACTIDIONE. (E.) Süss, R. (German Ctr. Cancer Res., Inst. Exp. Path., Heidelberg), M. Volm, V. Kinzel and R. Maurer. Experientia 25(6):629-630, 1969.

In NMRI mice treated with cycloheximide (CH; Actidione), no toxic effects were observed at a dose of 0.1 mg/g, but 3/10 mice died 24 hr. after admin. of 0.2 mg/g. In a quantitative Berenblum experiment in animals treated with 7,12-dimethylbenzanthracene (DMBA; 0.02 μ M) as initiator and phorbol ester A₁ (0.01 μ M) as cocarcinogen, tumor yields were unchanged. Binding of both DMBA and 3,4-benzpyrene by soluble skin proteins was reduced by CH, which also inhibited the synthesis of soluble skin proteins.

70-48 ULTRASTRUCTURAL STUDY OF 20-METHYL-CHOLANTHRENE-INDUCED SKIN CARCINOGENESIS, ESPECIALLY ON THE EARLY CHANGES. (Jap.) Saito, T. (Sapporo Med. Coll., Japan). Sapporo Med. J. (Sapporo Igaku Zasshi) 34(5):302-320, 1968.

In the skin of strain DD mice painted with 3-methylcholanthrene, the initial signs of cytotoxicity consisted of enlarged intercellular spaces and cytoplasmic blebs in the basal and prickle cell layers. The prickle cells showed degenerating mitochondria (which contained intracristal spherical granules) from the first day of treatment. In the proliferative stage, distortions of the differentiation and migration of the prickle cell layer led to disruption of the stratified epithelium. The number of keratohyalin granules increased during this stage, but decreased abruptly as the cells entered the carcinoma stage. The carcinoma cells showed an increased nuclear-cytoplasmic ratio, irregularly shaped nuclei, an increased vol. and number of nucleoli, an increase in cytoplasmic organelles (except for scanty desmosomes and tonofibrils), and some intercellular bundles of collagenous fiber. Keratohyalin granules in the carcinoma

cells were of 2 types: the rounded granules, surrounded by ribosomes, characteristic of the carcinoma cells; and irregularly shaped granules, associated with tonofibrils, also found in normal epithelial cells.

70-49 GENETIC DETERMINATION OF DIFFERENTIAL INFLAMMATORY REACTIVITY AND SUBCUTANEOUS TUMOR SUSCEPTIBILITY OF AKR/J AND C57BL/6J MICE TO 7,12-DIMETHYLBENZ[a]ANTHRACENE. (E.) Schmid, F. A. (Sloan-Kettering Inst. Cancer Res., New York, N. Y.), I. Elmer and G. S. Tarnowski. Cancer Res. 29(8):1585-1589, 1969.

Skin ulceration was induced in mice by application of 2-3 drops of 7,12-dimethylbenzanthracene (DMBA; 1.5%). Tumors were induced by a single s.c. inj. of DMBA (15 or 60 μ g in 0.2 ml sesame oil). Cross-breeding experiments showed that the previously described differential inflammatory reactivity of mice of strains AKR/J (low reacting) and C57BL/6J (high reacting) is controlled by a single pair of alleles. Incomplete dominance was seen in the high-reacting mice because of decreased penetrance in the heterozygous state, which was also shown by the less severe ulceration induced by DMBA in the (AKR/J x C57BL/6J)F₁ hybrids than in the C57BL/6J mice. Backcross studies confirmed a single-factor inheritance. Low-reacting strains have the H-2 alleles k and d, while high-reacting strains have the a, b and k H-2 alleles, suggesting that the alleles which control inflammatory reactivity do not correspond to the H-2 histocompatibility alleles. The low-reacting AKR/J mice were also less susceptible to s.c. tumor induction than the C57BL/6J mice. Further genetic studies suggested that, if the characteristics of inflammatory reactivity and s.c. tumor susceptibility are not identical, they are at least controlled by 2 closely linked genes on the same autosome.

70-50 CARCINOGEN-INDUCED NEOPLASIA WITH METASTASIS IN A SOUTH AMERICAN PRIMATE, Saguinus oedipus. (E.) Noyes, W. F. (Sloan-Kettering Inst. Cancer Res., New York, N. Y.). Proc. Soc. Exp. Biol. Med. 131(1):223-225, 1969.

One male and 1 female of 2 different species, the crested cottontop marmoset (Saguinus oedipus) and the white-lipped saddle-backed brown and black tamarin (Saguinus fuscicollis), were inj. s.c. with 3,4-benzpyrene (BP; 10 mg) and 7,12-dimethylbenzanthracene (DMBA; 10 mg in olive oil) on opposite flanks. Within 1 wk. of inj., both tamarins became anorexic, weak and debilitated; both died within 5 wk. Both marmosets developed hard nodules at the sites of inj., which became ulcerated at first but later healed. Within 16 mo., sarcomas developed at both sites: a spindle-cell sarcoma at the site of BP inj. and a rhabdomyosarcoma (with a metastasis to an inguinal lymph node) at the site of DMBA inj.

70-51 DELAYED HYPERSENSITIVITY TO CHEMICALLY INDUCED TUMORS IN MICE AND CORRELATION WITH AN IN VITRO TEST. (E.) Halliday, W. J. (U. Queensland, Australia) and M. Webb. J. Nat. Cancer Inst. 43(1):141-149, 1969.

Delayed hypersensitivity was induced in inbred CBA mice by inoc. of tumors which developed after a single inj. of 3-methylcholanthrene (0.5 mg s.c. in sesame oil), into mice of the same strain. Surgical removal of a transplanted growing tumor or admin. of disrupted tumor vaccine in Freund's adjuvant also induced sensitization. Delayed tumor-specific cutaneous reactions were seen when living tumor cells were inj. into the foot pads of sensitized mice. This in vivo hypersensitivity was correlated with specific susceptibility to inhibition of peritoneal cell migration in vitro.

70-52 EFFECT OF CHEMICAL CARCINOGENS ON VIRUS-INDUCED ROUS SARCOMA. (E.) Engle, C. G. (Rutgers U., New Brunswick, N. J.) and V. Groupé. Cancer Res. 29(7):1345-1349, 1969.

The cocarcinogenic effects of various carcinogens (when they were noted) in 3-day-old chicks infected with Rous sarcoma virus (RSV) were greatest when the test compound was inj. after RSV infection. The greatest enhancement of RSV-induced tumors was seen with 7,12-dimethylbenzanthracene. Inj. of N-2-fluorenylacetyamide before infection inhibited tumor development, while inj. after infection was cocarcinogenic. Enhancement was also seen with 7,12-dimethylbenzanthracene, 3,4-benzpyrene, 1,2,5,6-dibenzanthracene and (to a lesser extent) 3-methylcholanthrene. The chicks showed no alteration in gross or microscopic tumor morphology, no enhancement of secondary or metastatic tumors, and no secondary tumor development at the site of carcinogen inj.

70-53 INDUCTION OF MAMMARY AND OTHER SUBCUTANEOUS NEOPLASMS IN RATS BY 1-(4-DIMETHYLAMINO)BENZAL-INDENE. (E.) Roe, F. J. C. (Chester Beatty Res. Inst., London), R. L. Carter and N. A. Barron. Nature (London) 222(5191):383-384, 1969.

The tumorigenicity of 1-(4-dimethylaminobenzal) indene (DABI; 6 doses of 10 mg p.o. in 0.5 ml peanut oil at 2-3-day intervals) was studied in 6-wk.-old male and female Chester Beatty Wistar rats. The following tumors (mammary tumors, lipomas or s.c. sarcomas) developed in 16/18 females: 6 adenocarcinomas (first palpated after a mean of 8 mo.), 2 fibromyxosarcomas (mean 13 mo.), 6 fibroadenomas (mean 8 mo.), 2 lipomas (mean 5 mo.) and 1 adenocarcinoma (10 mo.). Tumors developing in 7/18 males included 1 adenocarcinoma (10 mo.), 4 fibromyxosarcomas (mean 4 mo.), 1 fibrosarcoma (12 mo.) and 1 pleomorphic

sarcoma (7 mo.). In controls (inj. with peanut oil only) fibroadenomas were seen in 2/12 females (11.5 mo.) and an adenoma in 1 female (14 mo.); no tumors were seen in 12 males. Two DABI-treated females and 8 treated males died (after 12 and 11 mo., resp.) without s.c. tumors (compared to 2 female and 9 male controls, after 15 and 13 mo; resp.). At 16 mo. after the beginning of treatment, all DABI-treated females had died; 3 treated and 3 control males were alive (none showed palpable tumors), and 7 control females were alive (1 showed a palpable s.c. tumor at 16 mo.). Internal neoplasms were seen in 3 DABI-treated females (1 malignant granulosa-cell tumor of the ovary at 15 mo.; 1 adrenal cortical adenoma at 12 mo.; 1 exocrine pancreatic adenoma at 13 mo.) and in 3 DABI-treated males (1 abdominal sarcoma at 15 mo.; 1 local lymphoma of the lung at 15 mo., 1 islet cell adenoma and 2 exocrine pancreatic adenomas at 15 mo.), but no internal tumors were seen in controls.

70-54 EFFECTS OF HYPOTHALAMIC AND AMYGDALOID LESIONS ON DEVELOPMENT AND GROWTH OF CARCINOGEN-INDUCED MAMMARY TUMORS IN THE FEMALE RAT. (E.) Welsch, C. W. (Michigan State U., East Lansing), J. A. Clemens and J. Meites. Cancer Res. 29(8):1541-1549, 1969.

In normal female Sprague-Dawley rats and rats with established 7,12-dimethylbenzanthracene-induced mammary tumors, marked stimulation of normal and neoplastic mammary tissue growth was seen in animals with bilateral median eminence lesions, especially in oophorectomized rats, suggesting that prolactin was responsible for these effects. Lesions in the preoptic area of the hypothalamus resulted in marked mammary tumor atrophy, including a marked decrease in the number of tumors/rat and in the mean tumor diameter; the lesions also caused a significant reduction in ovarian and uterine wt. and cessation of normal vaginal cycles. Amygdaloid lesions resulted in alteration of hypothalamic-pituitary function, which led to atrophy of mammary tumors, ovaries and uteri and the transformation of normal 4-5-day vaginal cycles to prolonged diestrus. The decreased ovarian and uterine wt. may reflect decreased estrogen secretion, which can lead to decreased prolactin secretion. Neither preoptic nor amygdaloid lesions caused any apparent regression of normal mammary tissue, suggesting a difference in the responsiveness of normal and neoplastic mammary tissues to these alterations in hormone balance. Most of the observed effects could be explained on the basis of alterations in secretion of pituitary prolactin.

70-55 LACTATE DEHYDROGENASE ISOZYMES OF 3:2'-DIMETHYL-4-AMINO BIPHENYL-INDUCED BREAST CARCINOMA. (E.) Brown, H. D. (Cancer Res. Ctr., Columbia, Mo.), S. K. Chattopadhyay, A. B. Patel, H. J. Spjut, J. S. Spratt, R. P. Pugh

and S. N. Pennington. Brit. J. Cancer 23(2): 446-451, 1969.

Poorly differentiated mammary adenocarcinomas (0.5-3 cm) were removed from 9 female white Wistar rats (< 3 mo. old at the beginning of the experiment), 8 mo. after the first inj. of 3'-2'-dimethyl-4-aminobiphenyl in peanut oil (2 mg/100 g x 5 d/wk. x 12 wk. s.c.; total 133-173 mg). Total cell homogenates, the soluble fraction, the endoplasmic reticulum fraction (100,000 x g pellet) and the nuclear fraction (20,000 x g pellet) from these tumors and from normal lactating rat mammary gland were studied for lactate dehydrogenase (LDH) isozyme activities. All tumor preparations showed LDH-V activities much higher than normal, and below-normal LDH-III activities. LDH-II and LDH-I, present in some of the normal tissue preparations, were not present in measurable amounts in any of the tumor preparations. By comparison to the normal preparations, the tumor preparations showed high LDH-IV activity in the total cell homogenates and cytoplasm, and low LDH-IV activity in the endoplasmic reticulum and particularly the nuclear fraction. The presence of discrete molecular populations in the tumor cells is suggested.

70-56 EFFECTS OF A CYCLIC STEROID CONTRACEPTIVE REGIMEN ON MAMMARY GLAND TUMOR INDUCTION IN RATS. (E.) Stern, E. (U. California Sch. Med., Los Angeles) and M. R. Mickey. Brit. J. Cancer 23(2):391-400, 1969.

A combination of norethynodrel (1 mg) x mestranol (40 µg; in 0.5 ml sesame oil) was admin. cyclically throughout life (to age 100-365 days; p.o.) to female Sprague-Dawley rats (approx. 45 days old), to simulate the intermittent schedule of oral contraception used by women. The onset of 7,12-dimethylbenz(a)anthracene (DMBA; 20 mg x 1 p.o. in 1 ml sesame oil at age 55 days) induced mammary tumors was delayed by this hormonal treatment, but the final number of tumors was not lower than the number found in vehicle-treated controls.

70-57 RELATIONSHIP BETWEEN PREVIOUS REPRODUCTIVE HISTORY AND CHEMICALLY INDUCED MAMMARY CANCER IN RATS. (E.) Moon, R. C. (U. Tennessee Med. Units, Memphis). Int. J. Cancer 4(3):312-317, 1969.

In virgin female Sprague-Dawley rats admin. 7,12-dimethylbenzanthracene (DMBA; 20 mg p.o. in sesame oil) at age 189-195 days, the mammary tumor incidence was 38.5% and the mean latent period (after DMBA admin.) was 82.2 days. No mammary tumors were seen in untreated virgin controls. In rats with histories of 1 pregnancy (beginning at age 50 days) with or without subsequent lactation, admin. of DMBA at age 189-195 days induced mammary tumors in 16.1% and

27.5%, resp., after mean latent periods of 128.2 and 111.4 days, resp. These 2 groups were not significantly different. In rats with histories of 2 pregnancies each, the mammary tumor incidence after DMBA admin. was 15.6% in rats without histories of lactation and 13.0% in rats with 1 lactation period after each pregnancy; mean latent periods were 130 and 180 days, resp. Most of the DMBA-induced mammary tumors were adenocarcinomas, with a few fibroadenomas and mixed tumors. Fibroadenomas appeared later than adenocarcinomas, but were fairly rare in both virgin rats and in animals with some combination of pregnancy and lactation.

70-58 COMPARATIVE STUDY OF LUNG CARCINOGENESIS, PROMOTING ACTION IN LEUKAEMOGENESIS AND INITIATING ACTION IN SKIN TUMORIGENESIS BY URETHANE, HYDRAZINE AND RELATED COMPOUNDS. (E.) Mirvish, S. S. (Weizmann Inst. Sci., Rehovot, Israel), L. Chen, N. Haran-Ghera and I. Berenblum. Int. J. Cancer 4(3):318-326, 1969.

In 6-8-wk.-old C57BL mice, exposed once to total-body irradiation (400 r) and given 10 i.p. inj. (1 inj./wk.) of the test compounds, N-hydroxyurethane (HU) showed the same coleukemogenic and lung carcinogenic (in non-irradiated mice) activity as an equivalent amount of urethane (U). Slight increases in the incidence of leukemia (mainly thymic) were also seen with acetyl-U and hydroxyurea. In SWR mice treated with 5 inj. of the test compounds and then painted with croton oil, the incidence of skin tumors was 32% with U, 8% with either HU or acetyl-U, and 4% in painted-untreated controls; the number of leukemias reflected a spontaneous incidence. The inactivity of methyl and n-propyl-hydroxycarbamates (nPHC) in the lung or skin tumor and leukemia systems suggested that the chemical specificity of U did not result from an ethyl-specific N-hydroxylating system. On a molar basis, hydrazine sulfate had about the same lung carcinogenic activity as U. A 61% incidence of lung adenomas (mean of 1.4 tumors/mouse) was seen in C57BL/6 mice receiving U; HU and acetyl-U had the same activity as U. In SWR mice, the tumor incidence was 100% with U (mean 12.7 tumors/mouse), HU and acetyl-U; N-methoxy-U, n-propyl carbamate (nPC) and hydrazine were also highly active. In C57BL/6 mice receiving a single inj. of the compounds, HU caused a more rapid and marked decrease in thymic wt. than U; nPHC had a definite transient effect, but nPC was almost inactive.

70-59 INCREASED INCIDENCE OF URETHANE-INDUCED LUNG ADENOMAS IN NEONATALLY THYMECTOMIZED MICE CHALLENGED WITH LYMPHOID CELLS. (E.) Trainin, N. (Weizmann Inst. Sci., Rehovot, Israel) and M. Linker-Israeli. Cancer Res. 29(10):1840-1845, 1969.

Albino Swiss mice, intact or thymectomized (thmx.) at age 3 days, were inj. either s.c.

(organ grafts) or i.p. (cell suspensions) with spleen, thymus or kidney tissue from 5-7-day-old Swiss mice, beginning at age 10 days (1 inj./wk.). One group of thmx. mice received irradiated spleen cells (10,000 r). All mice received 1 i.p. inj. of urethan (0.5 mg/g) at age 30 days. The mean number of lung adenomas was significantly higher in thmx. mice (3.4 tumors/mouse) than in intact mice (1.6 tumors/mouse). The incidence of lung adenomas was similar in mice receiving s.c. organ grafts or i.p. cell suspensions. Adenoma formation was increased in thmx. mice repeatedly treated with spleen (7.2 tumors/mouse) or thymic tissue (6.0 tumors/mouse), but the tumor incidence in mice inoc. with kidney cells or irradiated spleen cells (2.8 and 4.0 tumors/mouse, resp.) was similar to the incidence in thmx. controls (3.4 tumors/mouse). The increased tumor incidence and severity of pathology in mice inoc. with immunologically competent isogenic lymphoid cells suggested that repeated challenge with these cells may have initiated development of a graft-versus-host reaction. Recipients of immunologically competent cells also showed leukopenia, an impaired homograft response, lowered hemagglutinin titers and increased lymphoid pathology.

70-60 FINE STRUCTURE OF MURINE PULMONARY ADENOMATA INDUCED BY CARCINOGEN TREATMENT IN ORGAN CULTURE. (E.) Flaks, B. (U. Leeds Med. Sch., England) and A. Flaks. Cancer Res. 29(10):1781-1789, 1969.

Lung tissue explants from purebred BALB/c mice were exposed for 1-6 days *in vitro* to 3-methylcholanthrene (MC; 4 µg/ml), transferred to MC-free medium for 1 day, then implanted s.c. into isologous mice. During the next 3-12 mo., a large proportion of the mice developed tumors. The lamellar osmiophilic inclusion bodies noted in the tumor cells seemed morphologically identical to the specific inclusion bodies characteristic of Type II pulmonary alveolar cells (alveolar wall cells), suggesting that the *in vitro* induced adenomas originated from Type II alveolar cells. A large minority of the adenoma cells contained large, empty cytoplasmic clefts, which seemed to arise near the nuclei and to follow the contours of the nuclear surface. The nuclei constituted a large proportion of the tumor cell vol.

70-61 CELLULAR ANALYSIS OF LIVER CARCINOGENESIS. III. COMPARISON OF THE ULTRASTRUCTURE OF HYPERPLASTIC LIVER NODULES AND HEPATOCELLULAR CARCINOMAS INDUCED IN RAT LIVER BY 2-FLUORENYLACETAMIDE. (E.) Merkow, L. P. (U. Pittsburgh Sch. Med., Pa.), S. M. Epstein, E. Farber, M. Pardo and B. Bartus. J. Nat. Cancer Inst. 43(1):33-63, 1969.

White male Wistar rats were fed diets containing 2-fluorenylacetamide (FAA; 0.05%) for 9-48 wk. or more. Hyperplastic liver nodules were

grossly apparent after 9 or 15 wk. of FAA admin.; hepatocellular carcinomas with frequent local and distant (including intrathoracic) metastases developed in > 85% of the surviving animals after 48 wk. or more of treatment. Marked cell-to-cell uniformity was seen in the hyperplastic nodules, but they maintained the ability to respond ultrastructurally to a 24-hr. fasting stimulus. Both hyperplastic nodules and hepatomas showed annular lamellae, clustered and abundant smooth endoplasmic reticulum, and diminution of the parallel arrays in the rough endoplasmic reticulum.

70-62 α-FETOPROTEIN IN MONKEYS WITH HEPATOMA. (E.) Hull, E. W. (NCI, Bethesda, Md.), P. P. Carbone, D. Gitlin, R. W. O'Gara and M. G. Kelly. J. Nat. Cancer Inst. 42(6):1035-1044, 1969.

Hepatomas developed in 23/42 rhesus, cynomolgus and African green monkeys admin. N-nitrosodiethylamine (DENA), after a mean of 18 and 27 mo. after i.p. and p.o. treatment, resp. Serum α-fetoprotein (αFP) was detected in 20/23 tumor-bearing animals; 9/14 monkeys in a prospective study had positive αFP assays before or at the time of the development of palpable hepatic nodules. Once observed, αFP persisted at detectable levels until death or removal of the tumor. Serum αFP was not detected in 19/42 DENA-treated monkeys without tumors or in 75/75 monkeys that failed to develop hepatomas after treatment with 1-nitrosopiperidine, methylazoxymethanol (cycasin aglycone), aflatoxin B₁, 3'-methyl-4-dimethylaminoazobenzene, N-2-fluorenylacetamide or N,N'-2,7-fluorenylenebisacetamide.

70-63 A COMPARISON OF ELECTRON DENSITY AND HEPATOCARCINOGENIC ACTIVITY FOR VARIOUS DERIVATIVES OF 4-DIMETHYLAMINOAZOBENZENE. (E.) Brown, E. V. (U. Kentucky, Lexington) and W. H. Kipp. Cancer Res. 29(7):1341-1344, 1969.

In a series of 4'-alkyl-4-dimethylaminoazobenzenes and a series of prime-dimethyl-4-dimethylaminoazobenzenes, a relationship between the electron density at the amino nitrogen and hepatocarcinogenic activity in rats was found.

70-64 ULTRASTRUCTURAL ALTERATIONS OF THE CYTOMEMBRANES OF RAT PANCREATIC EXOCRINE CELLS INDUCED BY TREATMENT WITH 2-ACETYLAMINOFLUORENE. (E.) Flaks, B. (U. Bristol, England) and J. A. Moody. Europ. J. Cancer 5(3):231-238, 1969.

Male Leeds rats were fed a standard diet containing 2-acetylaminofluorene (AAF; 0.05% by wt.) for 3-4 wk. or 8-10 mo. before sacrifice; some rats were fed AAF for 10 mo., followed by 6 mo. on an

AAF-free diet. Electron microscopic examination of pancreatic acinar cells showed marked derangement of the endoplasmic reticulum (ER) and perinuclear cisternae, with dilatation of the cisternae and granules within the cisternae and ER. No evidence of detachment of ribosomes from the ER was observed. AAF had no apparent effect on the internal structure of the nuclei or nucleoli of the acinar cells, although the nuclei of some of the more severely affected cells showed irregularly indented surfaces.

70-65 OXIDATION OF CARCINOGENIC AZO-DYES.
III. METABOLITES OF DIMETHYLAMINO-AZOBENZENE IN THE BILE OF RATS. (E.) Marhold, J. (Res. Inst. Org. Synthesis, Pardubice-Rybitvi, Czechoslovakia), V. Rambousek, J. Pipalová and M. Matrká. Neoplasma (Bratisl.) 16(1):53-56, 1969.

After admin. of 4-dimethylaminoazobenzene (DAB; 1 g/kg) by a gastric tube to Wistar rats (VUFB, Rosice) the following metabolites were found in the bile: DAB, methylaminoazobenzene (MAB), aminobenzene (AB) 4'-hydroxy-AB, 4'-hydroxy-MAB, 4'-hydroxy-DAB, 2'-hydroxy-DAB and 2'-hydroxy-MAB. When DAB was admin. by portal inj., all of these compound except the 2'-hydroxy metabolites were found, together with an unknown compound which showed a light blue spot on chromatography.

70-66 ALKYLATION OF RAT LIVER NUCLEIC ACIDS NOT RELATED TO CARCINOGENESIS BY N-NITROSAMINES. (E.) Lijinsky, W. (U. Nebraska Coll. Med. Eppley Inst. Res. Cancer, Omaha) and A. E. Ross. J. Nat. Cancer Inst. 42(6):1095-1100, 1969.

In fasting male Wistar albino rats admin. ³H-labeled nitrosoazetidine, nitrosohexamethyleneimine, nitrosomethylaniline, or nitrosomethylcyclohexylamine (24-66 mg p.o.) and sacrificed 12-16 hr. later, no DNA's isolated from the livers contained an alkylated base derived from any of the compounds. No alkylated base was found in liver RNA's of animals admin. nitrosohexamethyleneimine or nitrosomethylaniline. However, 7-methylguanine was identified in the liver RNA of animals admin. nitrosomethylcyclohexylamine, and an alkylated base was also found in the RNA of nitrosoazetidine-treated animals.

70-67 INDUCTION OF TUMORS IN IRC MICE WITH N-NITROSOPIPERIDINE, ESPECIALLY IN FORESTOMACH. (E.) Takayama, S. (Cancer Inst., Tokyo). Naturwissenschaften 56(3):142, 1969.

Of 33 male ICR mice fed N-nitrosopiperidine (50 ppm in the diet) for 1 yr., 24/33 survived >12 mo. Tumors were found in the forestomach (squamous cell carcinoma; 18/24 surviving > 12 mo.), esophagus (papilloma; 2/24), liver (2 hepatocellular

carcinomas, 3 hemangioendotheliomas, 6 adenomas; 11/24) and lung (adenoma; 10/24). In untreated controls (28/30 survived 15 mo.), the tumors found included 2 lung adenomas and 1 lymphocytic leukemia.

70-68 INDUCTION OF INTESTINAL AND URINARY BLADDER CANCER IN RATS BY FEEDING BRACKEN FERN (Pteris aquilina). (E.) Pamukcu, A. M. (U. Ankara Coll. Vet. Med., Turkey) and J. M. Price. J. Nat. Cancer Inst. 43(1):275-281, 1969.

Albino rats (both sexes) fed pellets containing bracken fern (Pteris aquilina) from age 49 days (until death or sacrifice), and admin. Vitamin B₁ (2 mg/wk. s.c.) to offset thiaminase activity of the fern developed intestinal and urinary bladder tumors after the first 29 wk. Adenomatous polyps and adenocarcinomas were seen primarily in the ileum in 31/31 rats which died during the first 11 mo. Urinary bladder papillomas and carcinomas were observed in 81% of the rats autopsied. No tumors were seen in controls.

70-69 CARCINOGENICITY AND METABOLISM OF AROMATIC AMINES IN THE DOG. (E.) Deichmann, W. B. (U. Miami Sch. Med., Coral Gables) and J. L. Radomski. J. Nat. Cancer Inst. 43(1):263-269, 1969.

In female beagles, 2-naphthylamine (β-naphthylamine) was metabolized to the diester (di[2-amino-1-naphthyl]phosphate) and o-hydroxy conjugates, whereas 1-naphthylamine (α-naphthylamine) was metabolized to a monophosphate ester of 1-amino-2-naphthol and to p-hydroxy conjugates. Both compounds were N-hydroxylated, but β-naphthylamine was further oxidized to 2-nitrosomethylamine. In newborn mice inj. s.c. with 1- or 2-naphthylhydroxylamine and sacrificed after 14 mo., the 2-N-hydroxy derivative was more carcinogenic than the 1-N-hydroxy amine.

70-70 TRYPTOPHAN METABOLISM IN PATIENTS WITH BLADDER CANCER: GEOGRAPHICAL DIFFERENCES. (E.) Brown, R. R. (U. Wisconsin Med. Sch., Madison), J. M. Price, G. H. Friedell and S. W. Burney. J. Nat. Cancer Inst. 43(1):295-301, 1969.

After a loading dose of tryptophan (T), abnormal levels of urinary T metabolites were more frequent in a series of pts. with spontaneous bladder carcinoma from Wisconsin than in a group of similar pts. from the Boston area. The metabolism of T in the Boston pts. was similar to that seen in pts. with industrial bladder cancer. The differences between the Wisconsin and Boston groups did not appear to be related to variations in vitamin B6 nutrition or other factors known to affect T metabolism. It is

suggested that this difference may indicate some etiologic factor other than abnormal T metabolism, in the more industrial Boston environment.

70-71 PELLET IMPLANTATION STUDIES OF CARCINOGENIC COMPOUNDS. (E.) Bryan, G. T. (U. Wisconsin Med. Sch., Madison). J. Nat. Cancer Inst. 43(1):255-261, 1969.

In mice treated p.o. or s.c. with ^{14}C -labeled xanthurenic acid 8-methyl ether (XAE), most of the radioactivity was excreted in the urine as unchanged XAE within 24 hr. Very small quantities of 8-methoxy-4-hydroxyquinoline, 8-methoxy-quinolallic acid and an unidentified metabolite of XAE, were also found in the 24-hr. urine. Bladder pellet implants were made and elution curves derived for XAE in cholesterol (15 days), hexamethylbenzene (6 days), arachidic acid (6 days), stearic acid (31 days) and stearamide (154 days).

70-72 DEHYDROGENASES IN DIETHYLSTILBESTROL-INDUCED KIDNEY TUMORS OF THE SYRIAN HAMSTER. (E.) Krishna Murthy, A. S. (Child. Hosp., Boston, Mass.) and A. B. Russfield. Experientia 24(1):60-61, 1968.

Diethylstilbestrol pellets (20 mg) were implanted s.c. in an unspecified number of male Syrian hamsters, at intervals of 2 mo. The animals were sacrificed after 8 mo., revealing bilateral renal tumors (identified as benign tubular adenomas) in 2 animals. Sections (8 μ) were incubated in appropriate media and stained for the following oxidative enzymes; succinate (SUCC), glucose-6-phosphate (G-6-P), β -hydroxybutyrate (BHB) and isocitrate (ICIT) dehydrogenases (DH). In the normal kidney, cortical staining for all 4 enzymes was more intense than medullary staining. Staining for SUCC and BHB DH's was intense in the normal tissues and absent in tumor cells. Staining for G-6-P and ICIT DH's was more intense in the cytoplasm of the tumor cells than in the normal cells.

70-73 EFFECT OF UNILATERAL ORCHIECTOMY ON INDUCTION OF INTERSTITIAL CELL TUMORS IN BALB/c MICE. (E.) Canter, H. Y. (NCI, Bethesda, Md.) and M. B. Shimkin. Cancer Res. 28(2):386-387, 1968.

Intact or unilaterally orchietomized (orx.) 2 mo.-old BALB/c male mice were implanted s.c. with a 5-6-mg cholesterol pellet containing 10% diethylstilbestrol. Tumors of the right testis developed in 15/49 intact mice (mean age 10.3 mo.), tumors of the left testis developed in 19/49 (10.8 mo.), and 15/49 died without tumors (mean age 15.3 mo.). Tumors were seen in 57% of the mice and in 34.7% of testes. Following left orx., 17/44 developed tumors (39%; mean age

11.6 mo.) and 12/44 died without tumors (mean age 14.9 mo.). After right orx., 17/43 developed tumors (40%; mean 13.4 mo.) and 15/43 died without tumors (mean 15.3 mo.). Unilateral orx. did not affect the susceptibility of the remaining testis to interstitial cell tumor development (as compared to intact controls). Tumors developed in 57% of the intact animals and only 39% of the unilaterally orx. mice; this difference was statistically significant. The decreased tumorigenic response in unilaterally orx. animals was related to the reduction of the potentially responsive testicular cell mass.

70-74 THE INDUCTION OF MALIGNANT LYMPHOMAS AND OTHER TUMORS BY 7,12-DIMETHYLBENZ[a]ANTHRACENE IN THE SYRIAN GOLDEN HAMSTER. (E.) Toth, B. (U. Nebraska Coll. Med. Eppley Inst. Res. Cancer, Omaha). Cancer Res. 29(8):1476-1484, 1969.

The incidence of malignant lymphomas in adult Syrian golden hamsters inj. i.v. with 7,12-dimethylbenzanthracene (DMBA) was greater in animals receiving a single inj. of 3 mg (30% in females, 25% in males) than in animals receiving 4 weekly inj. of 3 mg each (18% and 7%, resp.). The 59 animals admin. 4 doses all died within 60 wk., while 45% of the 1-dose group and 81% of 200 controls (lymphomas were seen in 2% of the females and 7% of the males) were alive at this time. Three main types of malignant lymphomas were seen: stem cell or undifferentiated (6 animals), lymphocytic (8 animals) and histiocytic (11 animals). The stem cell and lymphocytic lymphomas were seen only in DMBA-treated hamsters (after mean latent periods of 34 and 46 wk., resp.); histiocytic lymphomas were seen in both treated and untreated hamsters (mean latent periods were 69 and 91 wk., resp.). In contrast to DMBA-induced mouse lymphomas, all of the observed malignant lymphomas were nonthymic and involved the spleen, kidney, liver, lymph nodes and even the bone marrow.

70-75 UNUSUAL ULTRASTRUCTURES IN A THYMIC LYMPHOMA OF AN X-RAY- AND URETHAN-TREATED X/Gf MOUSE. (E.) Goldfeder, A. (New York U., N. Y.) and A. K. Ghosh. Cancer Res. 29(10):1889-1892, 1969.

Total-body X-irradiation (300 r) and with 4 i.p. inj. of urethan (1 mg/g/wk., beginning 24 hr. after irradiation) were admin. to 150 mice (age 3 mo.). One male mouse of the inbred, naturally tumor-resistant X/Gf strain, which became moribund and was sacrificed at 7 mo., showed a unique thymic lymphoma with intracytoplasmic Type A virus particles. The lymphoblastic cells frequently contained nuclear projections surrounding areas of cytoplasm. The presence of macrophages produced a characteristic "starry-sky" appearance.

70-76 FINE STRUCTURE OF A TRANSPLANTED
CHEMICALLY INDUCED NONLYMPHOID THYMOMA.
(E.) Bockman, D. E. (Med. Coll. Ohio, Toledo)
and O. Stutman. Cancer Res. 29(9):1663-1668,
1969.

Nonlymphoid thymomas, originally induced by
intrathymic inj. of 7,12-dimethylbenzanthracene
in highly inbred newborn A mice, were inoc. s.c.
into syngeneic 5-wk.-old mice. These thymomas
were immunologically restorative in neonatally
thymectomized mice, but this capacity decreased
after serial transplantation. Electron micro-
scopic examination of a functional thymoma
showed a large number of cells with a dense
cytoplasmic matrix filled with single ribosomes
and polysomes. Many cells contained a moderate
amount of rough endoplasmic reticulum as well as
lipid droplets and lysosomes. Chromatin was
clumped both peripherally and centrally in round,
irregular nuclei. Type A virus particles were
observed only intracisternally. No cells were
seen that were identical in morphology with
normal thymic epithelial cells. No cells contained
bundles of cytoplasmic tonofilaments.

70-77 CHROMOSOMAL CHANGES ASSOCIATED WITH
URETHANE LEUKEMOGENESIS IN MICE. (E.)
Colnaghi, M. I. (Nat. Inst. Study Tumors, Milan,
Italy), G. Della Porta, G. Parmiani and G. Caprio.
Int. J. Cancer 4(3):327-333, 1969.

Mice of strains CTM, C3Hf, C57BL and SWR were
admin. 5 doses of urethan (U; 1 mg/g on alternate
days) from age 10-18 days; 1-3 hr. before sacrifice
(after varying times) they were inj. with
colchicine (0.5 mg i.p.). In thymic tissue
from untreated controls, most cells were diploid.
During U admin., few changes in ploidy were noted,
but chromosomal breaks, acentric fragments, and

metacentric, ring and unusually short or long
chromosomes were found. Most of these chromosomal
alterations became rare by 1 wk. after the end
termination of U admin., and were absent 5 and
11 wk. later. A bimodal distribution of 40 and
41 chromosomes was seen in 75/77 thymic lympho-
sarcomas; the 2 exceptional tumors were obtained
from male C3HF mice. In all metaphases with 41
chromosomes, the additional chromosome was
similar or identical to those of the smallest
pair.

70-78 STUDIES ON HYDROGEN EXCHANGE. X.
TRITIUM-LABELING OF CARCINOGENIC
4-NITROQUINOLINE 1-OXIDE AND RELATED COMPOUNDS.
(E.) Uehara, N. (Nat. Cancer Ctr. Res. Inst.,
Tokyo) and Y. Kawazoe. Chem. Pharm. Bull.
(Tokyo) 18(1):203-206, 1970.

70-79 NEW SOLVENT SYSTEMS FOR THIN-LAYER
CHROMATOGRAPHY OF AFLATOXINS. (E.)
Enstrom, G. W. (U.S. Dept. Agric., Ames, Iowa).
J. Chromatogr. 44(1):128-132, 1969.

70-80 BIOSYNTHESIS OF AFLATOXINS BY CELL-
FREE PREPARATIONS FROM Aspergillus
flavus. (E.) Raj, H. G. (U. Delhi Vallabhbhai
Patel Chest Inst., India), L. Viswanathan,
H. S. R. Murthy and T. A. Venkatasubramanian.
Experientia 25(11):1141-1142, 1969.

70-81 LACK OF INHIBITORY ACTION OF AFLATOXIN
ON THE INDUCTION OF DRUG-METABOLIZING
ACTIVITIES OF LIVER MICROSOMES BY PHENOBARBITOL.
(E.) Kato, R. (Nat. Inst. Hyg. Sci., Tokyo),
A. Takanaka, K. Onoda and Y. Omori. Jap. J.
Pharmacol. 19(3):470-472, 1969.

70-82 A SEQUENCE OF VIRUS-LIKE PARTICLE FORMATION IN THE ERGASTOPLASM OF GREENE'S MALIGNANT MELANOMA CELLS. (E.) Takahashi, M. (Wayne State U. Sch. Med., Detroit, Mich.) and Y. Mishima. Cancer 24(5):904-911, 1969.

Electron microscopic studies of Greene's melanotic melanoma (279A-XI) and amelanotic melanoma (278A-XI) from adult hamsters revealed distinctive spherical particles (diameter 90-110 m μ), consisting of an outer limiting membrane and a spherical, central, electron-dense nucleoid structure (diameter 40-50 m μ). This structure appeared to lack a limiting membrane, but it showed some substructure, as well as thin spoke-like rays which may be in contact with the outer limiting membrane. Several different particles were noted within the rough endoplasmic reticulum. Immature unorganized nucleoid structures, seen within the mildly bulging ergastoplasm, resembled aggregates of ribosomes and were in continuity with the ordered ribosomes of the surrounding ergastoplasm. In some cases, rows of typical mature virus-like particles (consisting of limiting membranes, distinct nucleoid structures and spoke-like rays) were seen within sacs of ergastoplasm. In no case were virus-like particles found in liver, kidney or skin of non-melanoma bearing control hamsters.

70-83 ULTRASTRUCTURAL STUDIES ON NORMAL AND LEUKAEMIC HUMAN HAEMATOPOIETIC CELLS. (E.) Ross, A. (Western Gen. Hosp. Cytogenetics Res. Unit, Edinburgh) and D. Harnden. Europ. J. Cancer 5(4):349-360, 1969.

Experimental material consisted of blood samples (BS) from 38 pts. with leukemia and 12 hematologically normal controls, bone marrow (BM) aspirations from 12 pts. with leukemia and 12 controls; plasma pellets (PP) from 2 pts. with leukemia and 1 control; and a lymph node biopsy from 1 pt. with chronic lymphatic leukemia. The types of leukemia studied were: chronic myeloid (13 BS, 9 BM, 1 PP); acute transformation of chronic myeloid (7 BS, 2 BM); acute myeloid (5 BS, 1 BM, 1 PP); acute monocytic (4 BS), acute lymphatic (5 BS) and chronic lymphatic (4 BS, 1 lymph node biopsy). Electron microscopic examination revealed no evidence of true virus particles in any preparation. The incidence of nuclear bodies and blebs was greater in leukemic cells than in normal cells. There was no difference between the 2 groups with respect to perichromatin granules.

70-84 IDENTIFICATION OF THE FILTRABLE LEUKOCYTE-TRANSFORMING FACTOR OF QIMR-WIL CELLS AS HERPES-LIKE VIRUS. (E.) Pope, J. H. (Queensland Inst. Med. Res., Brisbane, Australia), M. K. Horne and W. Scott. Int. J. Cancer 4(3):255-260, 1969.

The fetal human WBC-transforming factor from the QIMR-WIL human WBC cell line passed through a 200 m μ filter and showed a sensitivity to ether and high temperature similar to that of herpes viruses (previously reported). Human sera containing antibodies to the herpes-like virus (HLV) of the QIMR-WIL line were able to neutralize the transforming activity of this factor. Similar transformation was seen with filtrates of the Burkitt's lymphoma line QIMR-GOR, which also contains HLV.

70-85 VIRUSES IN HUMAN TUMORS. I. HODGKIN'S DISEASE. (E.) Stewart, S. E. (NCI, Bethesda, Md.), E. Z. Mitchell, J. J. Whang, W. R. Dunlop, T. Ben and S. Nomura. J. Nat. Cancer Inst. 43(1):1-14, 1969.

A cell culture (SS5) from a biopsy specimen from a 34-yr.-old man with Hodgkin's disease was divided at 8 and 14 wk. and then passaged for 15 mo. *in vitro*. The cells grew as free-floating clumps, singly or in pairs, and resembled primitive blast forms on staining. Two types of virus particles were identified: a herpes-type virus and another virus of about the same size. The latter virus was isolated by inoc. of WI38 cells with disrupted SS5 cells; passages were made at 1-2-wk. intervals for 6-12 mo. Multinucleated cells were seen 1 wk.-5 mo. after inoc., but extracellular viruses and large masses of a cytoplasmic filamentous component were not observed by electron microscopic examination until after 20 passages over 8 mo. Human lymphoblast cells, inoc. with virus from WI38 cultures, produced large quantities of virus with little cell destruction. The virus was hemadsorbed by guinea pig, chick, and monkey RBC; it grew on vervet monkey kidney cells, and induced encephalitis (fatal after 5-7 days) in weanling hamsters. This virus was serologically similar to SV5.

70-86 INVERSE RELATIONSHIP OF INTERFERON PRODUCTION AND VIRUS CONTENT IN CELL LINES FROM BURKITT'S LYMPHOMA AND ACUTE LEUKEMIAS. (E.) Swart, B. E. (NIH Div. Biol. Standards, Bethesda, Md.) and B. G. Young. J. Nat. Cancer Inst. 42(6):941-944, 1969.

Supernatants from Burkitt's lymphoma (EB1, EB2, EB3, AL1 and AL3) and acute leukemia (SK-L2 and SK-L3) cell line cultures were assayed for interferon by inoc. into HEP II and HA cells, which were challenged with vesicular stomatitis virus. Interferon titers (reciprocal of the highest dilution showing a 0.5log₁₀ yield reduction, compared with controls) were 1 with EB1 and EB2, zero with EB3, 0-1 with AL3, 4 with SK-L2 and 32-64 with AL1 and SK-L3. Cell lines with the highest titers of the herpes-like Epstein-Barr [EB] virus had the lowest interferon titers, suggesting that the EB virus may be unrelated to the initial induction of interferon.

70-87 ANTIBODIES IN PATIENTS WITH BURKITT'S TUMOR AND LEUKEMIA: COMPARISON OF TWO FLUORESCENCE TESTS. (E.) Goldman, M. (Bionetics Res. Labs., Kensington, Md.), H. F. Bushar and J. I. Reisher. Int. J. Cancer 4(5):666-670, 1969.

Sera from 63 pts. with Burkitt's lymphoma (14) or leukemia (49) and 69 normal controls were studied by membrane (MF) and cytoplasmic fluorescence (cyto-F) tests. The antigens employed were 4 lymphoblastic cultures, 2 positive for herpes-type virus (HTV) (P3 and F152) and 2 negative for HTV (P1 and N37). Tests were negative with HTV-free cell lines, but the level of positivity was much lower in HTV-positive sera measured by the MF test than when measured by the cyto-F procedure. Internal controls suggested that the observed differences did not result from improper functioning of either test. The results supported the hypothesis that 2 different antigen systems must be involved in the MF and cyto-F procedures, although the possibility that each test may indicate different aspects of the same disease process was not excluded.

70-88 HERPES-TYPE VIRUS PARTICLES AND CHROMOSOME MARKERS IN TWO HUMAN CELL LINES DERIVED FROM EMBRYONIC CULTURES EXPOSED TO HUMAN LEUKEMIC CULTURE FLUID IN VITRO. (E.) Ito, Y. (Aichi Cancer Ctr. Res. Inst., Nagoya, Japan), I. Kimura, Y. Kurita and T. Osato. Gann 60(3):247-251, 1969.

Electron microscopic examination of 2 human embryo cell lines (THE-2 and THE-3), derived from cultures morphologically altered after in vitro exposure to a cell-free supernatant of human leukemic culture fluid, showed herpes-type virus particles. These virus particles were morphologically identical in both cell strains, but occurred more frequently in THE-3 cells. Virus particles were seen most often in the nucleus and cytoplasm of degenerating cells, and resembled those seen in cultured Burkitt's lymphoma cells and in some American leukemic cell lines. The THE-2 cell line consisted of small, round, relatively uniform cells, while the THE-3 cell line consisted of a mixed population of several morphologically different cells, including large polygonal cells with a prominent nucleolus. The C10 chromosomal marker was seen in 10% of the THE-2 and 45% of the THE-3 cells. THE-2 cells had a mode of 46 XX chromosomes. THE-3 cells had 2 modes (48 and 49 chromosomes); all analyzed cells were XY.

70-89 INFECTIOUS MONONUCLEOSIS, LYMPHOBLASTIC LEUKEMIA, AND THE E. B. VIRUS. (E.) Ragab, A. H. and T. J. Vietti (500 South Kingshighway, St. Louis, Mo.). Cancer 24(2):261-265, 1969.

A 10-yr.-old girl with acute lymphoblastic leukemia developed infectious mononucleosis (IM) 6 wk. after the diagnosis of leukemia (during remission). The titer of EB virus antibody in serum collected before IM infection was < 1:10; however, the titer rose to 1:160, 22 days after the onset of fever.

70-90 DETECTION OF A SMALL VIRUS IN A CULTIVATED HUMAN WILMS' TUMOR. (E.) Smith, J. W. (St. Jude Children's Res. Hosp., Memphis, Tenn.), D. Pinkel and S. Dabrowski. Cancer 24(3):527-534, 1969.

Electron microscopic examination of "spontaneously transformed" cells from a Wilms' tumor, cultivated in vitro for 15 mo. after removal from a 16-mo.-old boy, demonstrated a small virus particle, which resembled a papova virus by its size (45-50 mμ in diameter), its electron-dense nucleoid and the presence of a closely adherent, double external membrane. Viral replication was seen only in the cells where the virus was first observed. Attempts to establish in vitro or in vivo activity of this virus were unsuccessful.

70-91 CULTIVATION OF A FILTERABLE AGENT ASSOCIATED WITH MAREK'S DISEASE. (E.) Cook, M. K. (Nat. Inst. Allergy Infect. Dis., Bethesda, Md.). J. Nat. Cancer Inst. 43(1):203-212, 1969.

A virus component was consistently isolated from the CAL-1 strain of Marek's disease. The component was about 100 mμ in diameter and produced a syncytial type of CPE in chick embryo fibroblasts. It was resistant to 5-iodo-2'-deoxyuridine (50-250 μg/ml), inactivated by ether and chloroform, and was negative in the complement fixation for avian leukosis. Filtrates of the tissue culture virus, grown intra-abdominally in 1-day-old white Leghorn chicks, induced a disease resembling Marek's disease.

70-92 THE ONCOGENIC EFFECTS OF NONTRANSFORMING VIRUSES FROM AVIAN MYELOBLASTOSIS VIRUS. (E.) Smith, R. E. (VA Hosp., Gainesville, Fla.) and C. Moscovici. Cancer Res. 29(7):1356-1366, 1969.

Isolation of several leukosis viruses of subgroups A and B from standard avian myeloblastosis virus (AMV; BAI strain A) is described. A high incidence of osteopetrosis was seen in 11-day-old chick embryos inj. i.v. with subgroup A virus derived from a Japanese quail (Coturnix coturnix japonica) with an AMV-induced lymphoma. A subgroup B virus, collected from chickens with AMV-induced leukemia and propagated in C/O fibroblast cultures, induced osteopetrosis and nephroblastomas in 11-day-old chick embryos. Inj. of a strain from a quail rhabdomyosarcoma

caused a high incidence of lymphoid leukosis and a low incidence of osteopetrosis and nephroblastoma. Inj. of another subgroup A strain, without passage through the quail, caused lymphoid leukosis, nephroblastoma and rhabdomyosarcoma. None of the AMV-derived strains caused leukemia or *in vitro* malignant transformation of hematopoietic tissues in any systems tested. Immunological cross-reactivity was seen between all subgroup A isolates and between all subgroup B isolates, but not between subgroups A and B. Only subgroup A strains were isolated from quail tumors.

70-93 INFECTION OF HUMAN EMBRYONIC CELL CULTURES WITH THE RAUSCHER MURINE LEUKEMIA VIRUS. (E.) Wright, B. S. (Chas. Pfizer & Co., Inc., John L. Smith Mem. Cancer Res., Maywood, N. J.) and W. Korol. Cancer Res. 29(10):1886-1888, 1969.

Five wk. after addition of Rauscher mouse plasma virus (HL-67-4) to monolayer cultures of human embryonic muscle cells (G8-6), electron microscopic examination showed virus particles budding from the plasma membrane and extracellular "C-type" particles. Newborn and weanling BALB/c mice, inoc. i.p. with concentrated extracellular virus, showed no evidence of any typical Rauscher virus disease symptoms after 3 mo. Human cell-derived G8-6 virus was infectious when subpassaged at least once to control G8-6 cells, several other human embryonic cultures and to the JLS-V9 mouse cell line. The virus produced in infected G8-6 cell cultures was similar to the mouse plasma virus in morphology and density.

70-94 TRANSFORMATION OF HAMSTER EMBRYO CELLS *IN VITRO* BY RAUSCHER LEUKEMIA VIRUS. (E.) Rhim, J. S. (NCI, Bethesda, Md.), R. J. Huebner and R. C. Ting. J. Nat. Cancer Inst. 42(6):1053-1060, 1969.

In primary suspension cultures of hamster embryo cells infected with Rauscher leukemia virus and grown as monolayer cultures, the first abnormal growth was noted after 44 days, consisting of a few isolated foci of tightly packed epithelioid cells, which enlarged rapidly to form colonies. Cell lines were obtained and maintained for 10 mo. (45 cell transfer passages). During this time, the cultures produced group-specific complement-fixing antigen and virus infectious for mouse, rat and hamster embryo cells. Both X-irradiated (350 r) and non-irradiated 4-wk.-old hamsters, inoc. with transformed cells, developed fibrosarcomas with an av. latent period of 15-25 days. Cells derived from these tumors could be re-established in tissue culture.

70-95 TRANSMISSION OF RAUSCHER LEUKEMIA IN MICE. (E.) Mirand, A. G. (Roswell Park Mem. Inst., Buffalo, N. Y.) and E. A. Mirand. Experientia 25(8):829-830, 1969.

Newborn Ha/ICR Swiss mice were inj. s.c. with various body fluids, tissue extracts, and feces from Rauscher leukemia virus (RLV)-infected isogeneic male and female mice; the specimens were collected during the first 1 mo. after RLV infection of the donors. The mean leukemia incidence in the recipients was 97% with blood, 84% with milk, 5% with urine and semen; 90% with spleen, 93% with liver and 7% with brain. Leukemia was not transmitted by embryo extracts; saliva or feces. In reciprocal foster-nursing experiments, transmission of RLV by the milk was seen in 13/69 offspring (18.9%) of normal mice foster-nursed by infected females. Leukemia did not develop in the offspring of infected mothers nursed by normal females. The earliest development of leukemia was seen at 3 mo. Non-infected mice failed to develop leukemia when kept in continuous contact with RLV-inj. littermates.

70-96 THE INFLUENCE OF STRESS ON MURINE LEUKEMIA VIRUS INFECTION. (E.) Jensen, M. M. (U. California Los Angeles Sch. Med.). Proc. Soc. Exp. Biol. Med. 127(2): 610-614, 1968.

Various stresses were inflicted on 6-8-wk.-old inbred female Swiss Webster-BRVS mice inj. with Rauscher leukemia virus (RLV). Mice subjected to 10-daily periods of sound stress or to avoidance-learning stress before i.v. inj. of RLV, showed a significant retardation of splenic enlargement. Another group showed significant retardation in spleen size when stress was applied after, but not before, inoc. of RLV. The difference in mean wt. between stressed (20.9 g) and control (21.3 g) mice was significant. In another group subjected to avoidance-learning stress (for 5 days), followed by adrenalectomy (adx.) and a 1-day rest before RLV inj. (i.v.) with RLV, then stressed again (for 13 days) and sacrificed, a significant difference in spleen size was seen between stressed and control intact mice, but not between stressed and control adx. mice. Death rates were lower in stressed mice. No correlation was observed between the effectiveness of stress and splenic colony-forming titers, plasma virus contents or splenic histology. No significant differences were seen between intact and adx. infected mice, when both groups were treated s.c. with 6-mercaptopurine (30 mg/kg/inj.), triethylene melamine (0.5 mg/kg) or a terephthalanilide compound (50 mg/kg) at 2-day intervals through day 16 after FLV inoc.

70-97 EFFECTIVE ANTIVIRAL THERAPY OF TWO MURINE LEUKEMIAS WITH AN INTERFERON-INDUCING SYNTHETIC CARBOXYLATE COPOLYMER. (E.) Chirigos, M. A. (NCI, Bethesda, Md.), W. Turner, J. Pearson and W. Griffin. Int. J. Cancer 4(3):267-278, 1969.

Inj. of a copolymer (NSC-46015; pyran-2-succinic anhydride, 4,5-dicarboxytetrahydro-6-methyl-, anhydride, polymers) induced interferon production in 6-8-wk.-old BALB/c mice. The protective value of induced interferon was studied in Friend leukemia virus- (FLV) and Rauscher leukemia virus (RLV)-infected mice receiving the copolymer (25 mg/kg/day was more effective than single doses of up to 400 mg/kg). Pretreatment with copolymer retarded PLV and RLV-induced spleen foci, splenomegaly and viremia, and caused marked increases in the mean survival times. The degree of protection was related to the dose of infecting virus. Treatment with the copolymer was not effective when started after virus infection.

70-98 DISAPPEARANCE OF INFECTIOUS VIRUS FROM FRIEND VIRUS-INDUCED C57BL/6 TUMORS. (E.) Odaka, T. (Inst. Med. Sci., Tokyo), Y. Ikawa and K. Takizawa. Int. J. Cancer 4(4): 403-415, 1969.

When C57BL/6 mice were inj. i.p. with Friend leukemia virus (FLV) within the first 2 wk. of life, hepatosplenomegaly and enlarged mesenteric lymph nodes developed within 2 mo. Infectious virus was found in the spleens of all diseased mice; the spleens also showed subcapsular infiltrations of lymphoblastic lymphoma, partly with a "starry-sky" pattern. When spleen fragments from mice with enlargement of the mesenteric lymph nodes and/or thymus were grafted into syngeneic mice, 5/5 hosts developed solid tumors at the graft sites. These solid tumors were also of the "starry-sky" histological pattern and showed a tendency to lymphocytic maturation in the peripheral portion of the tumors. No tumors were induced by grafts of spleens from mice without enlarged mesenteric nodes and thymus. In 4 tumor lines, FLV activity disappeared within a few passages in C57BL/6 mice, but virus-specific transplantation antigens could be demonstrated in some of these tumors.

70-99 SPONTANEOUS HEMATOPOIETIC RECOVERY OF FRIEND VIRUS-INFECTED MICE AFTER HEAVY X IRRADIATION. (E.) Gallien-Lartigue, O. (Radium Inst., Orsay, France), P. Tambourin, F. Wendling and P. Zajdela. J. Nat. Cancer Inst. 42(6):1061-1068, 1969.

Male and female Swiss mice (3 mo. old) infected i.p. with Friend leukemia virus (FLV; 0.2 ml of 1% wt./vol. spleen extract), 15 days before total-body X-irradiation (950 r, showed endogenous hematopoietic recovery after irradiation. Animals infected with FLV 6 days before irradiation (as above) showed no hematopoietic recovery, and mortality curves were similar to those seen in noninfected, irradiated controls. Survivors of both groups showed a longer survival time than FLV-infected, non-irradiated controls.

70-100 TRANSPLANTABLE FRIEND VIRUS-INDUCED TUMORS IN RATS. (E.) Kobayashi, H. (Hokkaido U. Sch. Med. Cancer Inst., Sapporo, Japan), M. Hosokawa, N. Takeichi, F. Sendo and T. Kodama. Cancer Res. 29(7):1385-1392, 1969.

Four lines of transplantable tumors were produced in Wistar-King-Aptekman/Mk rats inoc. at birth with Friend leukemia virus (FLV). Three lines were lymphosarcomas (WFT-1, WFT-3, WFT-4); WFT-1 resembled Burkitt's lymphoma, while WFT-2 was apparently a reticulum cell sarcoma. RFT cells proliferated in isologous rats conditioned with FLV at birth, or with irradiation, but not in isologous non-conditioned rats. When the tumor cells were transplanted s.c., they grew at the inj. site, in regional lymph nodes and in remote organs. Only WFT-3 was maintained in both solid and ascitic forms.

70-101 RAT VIRUS-MEDIATED SUPPRESSION OF LEUKEMIA INDUCTION BY MOLONEY VIRUS IN RATS. (E.) Bergs, V. V. (U. Miami Sch. Med., Coral Gables, Fla.). Cancer Res. 29(9):1669-1672, 1969.

Rats were inoc. i.p. at birth with a mixture of Moloney leukemia virus (MLV) and rat virus (RV), strain RV-13 or 9HV-B. In Sprague-Dawley rats, the incidence of leukemia was 100% in those receiving MLV only and 67% in those receiving MLV (10^2 ID₅₀/0.1 ml) + 9HV-B (10^5 TCID₅₀/0.1 ml); with MLV titers of 10^1 ID₅₀/0.1 ml, the incidence was 62% in rats admin. MLV only, 23% in rats receiving MLV + 9HV-B (as above), and 17 in rats receiving MLV + RV-13 (as above). In W/FU rats inoc. with MLV only (10^2 ID₅₀/0.1 ml), the leukemia incidence was 95% compared to 60% with MLV and 9HV-B. Hemagglutination inhibition (HI) titers against RV-13 were low in leukemic and nonleukemic rats inj. with MLV only; HI titers were generally higher in nonleukemic rats inj. with MLV + RV than in leukemic rats. The possibility of reciprocal inhibition between MLV and RV in rats is suggested.

70-102 EFFECT OF ANTILYMPHOCYTIC AND ANTI-THYMOCYTIC SERA ON THE DEVELOPMENT OF MOUSE LYMPHOMA. (E.) Vredevoe, D. L. (U. California Sch. Nursing Lab. Nucl. Med. Radiat. Biol., Los Angeles) and E. F. Hays. Cancer Res. 29(9):1685-1690, 1969.

Antilymphocytic serum (ALS) was more effective than 6-mercaptopurine (6-MP; 100 mg/kg diet) or azathioprine (150 mg/kg in diet or 150 mg/kg i.p.) in suppressing hemagglutinins to sheep RBC in AKR and C3H/HeJ mice. A significant increase in the development of lymphomas was seen in adult C3H/HeJ admin. a prolonged course of ALS simultaneously with 4 inj. of Gross leukemia virus (GLV), 6-MP and azathioprine did not increase the lymphoma incidence. A single

inj. of GLV, preceded or followed by treatment with antithymocytic serum (ATS), did not induce lymphomas in adult C3H/HeJ mice. The prolonged latent periods for lymphoma development, in mice inj. with C3H/HeJ ATS, suggested that this ATS may inactivate prelymphoma or lymphoma cells during the latent period of spontaneous lymphoma in AKR mice or GLV-induced lymphoma in C3H/HeJ mice. ATS may also suppress mechanisms involved in the elimination of multiple doses of lymphoma virus (inj. i.p.) in C3H/HeJ mice, and rejection of allogeneic tumor tissue.

- 70-103 NEUROLOGICAL ILLNESS AFTER INOCULATION OF TISSUE FROM TUMOUR BEARING ANIMALS. (E.) Field, E. J. (MRC Demyelinating Dis. Unit., Newcastle upon Tyne, England), D. H. Adams and G. Joyce. Nature (London) 221(5187):1265-1266, 1969.

Plasma from a mouse, inj. (i.p.) 3 mo. previously with the Riley agent (lactate dehydrogenase-elevating virus) from a mouse with Ehrlich ascites carcinoma (EAC), was inj. i.p. into 17 Swiss mice (4-6 wk. old). In these and other mice, neurological disease was found within 6-11 mo., including astrogliosis of the spinal gray matter and vacuolization of the white tracts. In all cases transfer was mediated by plasma and was associated with leukemia. Similar results were seen in mice inj. with brain tissue from a mouse with EAC. The inability to pass the disease by inj. of brain and spinal cord from other EAC-bearing animals, suggested that the initial series may have been contaminated by scrapie.

- 70-104 A TRANSMISSIBLE VIRUS-INDUCED LYMPHOCYTIC LEUKEMIA OF THE CAT. (E.) Rickard, C. G. (Cornell U. New York State Vet. Coll., Ithaca), J. E. Post, F. Noronha and L. M. Barr. J. Nat. Cancer Inst. 42(6):987-1014, 1969.

Cellular and cell-free preparations of a spontaneous thymic lymphocytic leukemia, obtained from a 5-yr.-old castrated male cat, induced leukemia in 0-3-day-old kittens. Cell-free preparations were leukemogenic through 7 serial passages, with a median latent period of 53 days in 56/68 inoc. kittens which died with leukemia; 5/68 died of other diseases 41-50 days after inoc., and 7/68 survived. Cats with experimentally induced leukemia showed numerous Type C virus particles, with buds in certain tissues. Leukemic lesions were found at death (104 and 136 days old, resp.) in 2/25 non-inoc. littermates; 1/19 living controls showed evidence of Type C virus particles in the bone marrow biopsy, and blood from this animal induced similar leukemic lesions (with Type C particles) when inj. into newborn kittens.

- 70-105 REPLICATION OF CAT LEUKAEMIA VIRUS IN CELL SUSPENSION CULTURES. (E.)

Theilen, G. H. (U. California Sch. Vet. Med., Davis), T. G. Kawakami, J. D. Rush and R. J. Munn. Nature (London) 222(5193):589-590, 1969.

A leukemia virus was isolated by differential centrifugation from tissue of a 3-yr.-old cat with spontaneous leukemia. Within 8 wk., leukemia developed in 3/5 1-day-old kittens inoc. i.p. with 2.3 g equivalents of the viral concentrate. When the virus was repassaged from 2 of the newly infected kittens into 4 other 1-day-old kittens, leukemia developed in 2/4 recipients after 40 wk.; another recipient developed a progressive anemia, with almost complete replacement of the bone marrow by malignant lymphocytes. Cell cultures from a solitary kidney tumor from this animal grew singly or in aggregates; they were typically lymphoid (diameter of 10-13 μ , with nucleus of 7-10 μ) and had a generation time of 36 hr. Type C virus particles were found, budding from the plasma and vacuolar membranes of these cells. This suspension may be a better source of Type C cat leukemogenic virus than particles budding from cells grown in monolayer cultures.

- 70-106 FRIEND VIRUS-INDUCED RETICULUM CELL SARCOMAS GROWN IN VITRO: FURTHER EVIDENCE FOR THE ABSENCE OF FRIEND VIRUS. (E.) Fieldsteel, A. H. (Stanford Res. Inst., Menlo Park, Calif.), C. Kurahara and P. J. Dawson. Cancer Res. 29(10):1846-1850, 1969.

An attempt was made to identify Friend virus (FV) in tissue cultures of FV-induced reticulum cell sarcomas from BALB/c and BDF₁ mice. Criteria for the absence of virus from the BALB/c cultures were repeated inability to recover infectious virus; inability of the culture to induce neutralizing antibody to FV; and failure of conc. culture fluid or cell lysates to protect mice against small doses of FV. Small numbers of Type A virus particles were seen in electron micrographs, but no Type C particles. The BDF₁ culture also appeared to be free of infectious virus.

- 70-107 MURINE SARCOMA VIRUS: TITRATION PATTERNS AND INTERFERENCE BY A MURINE LEUKEMIA VIRUS. (E.) Somers, K. D. (U. Chicago, Ill.) and W. H. Kirsten. Int. J. Cancer 4(5):697-704, 1969.

A mouse sarcoma virus (MSV-K) was isolated from a rat-adapted mouse erythroblastosis virus (MEV) and assayed by focus formation in 3T3 cell cultures. MEV could be assayed *in vitro* by its ability to interfere with focus formation by MSV-K. This interference was initially detected 14 days after infection; max. resistance to MSV-K challenge was seen at 21 days. The late onset of interference was attributed to the low multiplicities of virus employed. The MEV-induced interference was specific for MSV-K and was not due to interferon. MSV-K from transformed

3T3 cells showed "1-1h1" titration patterns; the ratio of MEV to MSV was 10:1. It is suggested that a single MSV-K particle can produce a focus of altered cells without simultaneous infection with a separate particle of MEV.

- 70-108 STUDIES ON MURINE SARCOMA VIRUS: ANTIGENIC CHARACTERIZATION OF MURINE SARCOMA VIRUS INDUCED TUMOR CELLS. (E.) Chuat, J.-C. (Saint Louis Hosp. Inst. Leukemia Res., Paris), L. Berman, P. Gunvén and E. Klein. Int. J. Cancer 4(4):465-479, 1969.

Membrane fluorescence, serum absorption, colony-inhibition and transplantation immunity methods were used for antigenic characterization of mouse sarcoma virus (MSV)-transformed mouse, rat and hamster cells. Complete immunological cross-reactivity was seen between MSV-Moloney (MSV-M) and MSV-Harvey (MSV-H) and between Moloney leukemia virus (MLV) and MSV. Immunization against either MSV-H or MSV-M elicited antibodies reacting with both MSV-H- and MSV-M-induced tumor cells; immunization with either MSV- or MLV- detected antigens on MLV-induced lymphoma or MSV-induced sarcoma cells. Cross-absorption studies suggested a close relationship between MSV and MLV.

- 70-109 PREVENTION OF CARCINOGENESIS BY MURINE SARCOMA VIRUS (HARVEY) FOLLOWING INJECTIONS OF IMMUNE SERA DURING THE LATENT PERIOD. (E.) Bubeník, J. (Czechoslovak Acad. Sci. Inst. Exp. Biol. Genet., Prague), A. Turano and G. Fadda. Int. J. Cancer 4(5):648-654, 1969.

Immune sera were prepared by immunization of mice and rats with mouse sarcoma virus (MSV-Harvey) or with irradiated tissue of MSV-induced tumors. About the same results were obtained with sera of different origins (inbred or outbred mice, outbred rats) immunized with various MSV-containing antigen preparations. Carcinogenesis was blocked in mice (A/L, C57Bl/6 and Swiss) and rats (Wistar), inoc. at birth with MSV, by repeated treatment with isologous, homologous or heterologous immune sera. Tumor inhibition was highest with sera containing the highest levels of virus-neutralizing antibodies (VNA). Antibodies with tumor-specific transplantation antigen (TSTA) specificities were found solely in some of the immune sera which inhibited carcinogenesis. No correlation was apparent between the capacity of the sera to prevent MSV carcinogenesis and to influence the growth of MSV-induced tumor cells, or between the TSTA and the VNA levels in the immune sera. It is concluded that VNA, rather than TSTA, were responsible for the prevention of MSV carcinogenesis.

- 70-110 MYO-INOSITOL INFLUENCES RELEASE AND INACTIVATION OF MURINE SARCOMA VIRUS

FROM DESICCATED TRANSFORMED MOUSE EMBRYO CELLS. (E.) Bather, R. (U. Saskatchewan, Saskatoon, Canada) and J. Yang. Nature (London) 222(5193): 589, 1969.

Mouse embryo cells transformed by Moloney sarcoma virus (MSV) were treated with myo-inositol (5%) and desiccated at relative humidities of 30-70%. With the exception of 30% humidity, MSV yields were higher than in untreated cells. The yield at 60% humidity was 2-3-fold higher than the yield from control cultures.

- 70-111 ENHANCING EFFECT OF THE MURINE SARCOMA VIRUS (MSV) ON THE REPLICATION OF THE MOUSE HEPATITIS VIRUS (MHV) IN VITRO. (E.) Chany, C. (St. Vincent de Paul Hosp., Paris) and F. Robbe-Maridor. Proc. Soc. Exp. Biol. Med. 131(1):30-35, 1969.

When cultures of Balb/c mouse embryo fibroblasts (MEF) were infected with Moloney mouse sarcoma virus (MSV) 24 hr. before or simultaneously with infection with mouse hepatitis virus (MHV), a significant increase in the yield of infectious MHV was noted, an effect probably induced by the MSV genome. The tumor-enhancing properties of MSV were more sensitive to UV radiation (10,000 ergs/mm²) than was its tumorigenicity. When MEF cells were treated simultaneously with MSV and actinomycin D (0.01 or 0.05 µg) for 18 hr., the enhancement of MHV was only 28% of that seen in controls; simultaneous exposure to puromycin (2 µg) completely blocked enhancement. It is suggested that the integrity of the viral genome and the functional integrity of the cellular ribosomes are required for the enhancing effects of MSV. It is concluded that MSV seems to block the action of interferon.

- 70-112 ROUS SARCOMAS IN MICE: THE CHROMOSOMAL PROGRESSION IN PRIMARY TUMOURS. (E.) Mark, J. (U. Lund Inst. Genet., Sweden). Europ. J. Cancer 5(4):307-315, 1969.

Newborn inbred DBA mice were inj. with a finely minced suspension of Rous chicken sarcoma, strain RSV-SR. Chromosomal progression studies were performed in specimens from 11 sarcomas, which were partly excised and allowed to recur. Five tumors with an initially diploid stemline, underwent heteroploid transformation, beginning with the formation of a few variant cell types which deviated numerically and/or structurally from the normal diploid stemline. In the next phase of transformation, a heteroploid sideline took over the diploid stemline. The last phase comprised modification of the heteroploid sideline, without a departure from the initially established progressional pathway of the individual tumor. The 4 possible pathways consisted of hypodiploid stemlines (with no common characteristics of progression),

pseudodiploid stemlines (with progressively increasing numerical and structural pleomorphism), hyperdiploid stemlines and polyploid stemlines (with a trend toward triploidy).

- 70-113 INACTIVATION OF ROUS SARCOMA VIRUS PREPARATIONS DETECTED BY DENSITY GRADIENT CENTRIFUGATION. (E.) Smida, J. (Cancer Res. Inst., Bratislava, Czechoslovakia) and V. Smidová. Neoplasma (Bratisl.) 16(1):101-103, 1969.

Preparations of the Schmidt-Ruppin (SR) and Bryan standard strains of Rous sarcoma virus (RSV) were made from chicks and from *in vitro* transformed chick embryos. After heating (37°C) and exposure to antisera, the virus samples showed a change in the number, density, character and infectivity of light-scattering bands after ultracentrifugation. All heated samples showed a marked shift towards lower densities and a rapid loss of infectivity. Treatment of SR-RSV produced 2 bands, slightly differing in density from control preparations, both with markedly reduced infectivity.

- 70-114 TRANSMISSION OF MAMMARY TUMOR VIRUS BY FEMALE GR MICE: RESULTS OF EGG TRANSPLANTATION. (E.) Zeilmaker, G. H. (Netherlands Cancer Inst., Amsterdam). Int. J. Cancer 4(3):261-266, 1969.

Pronuclear eggs and blastocysts from GRS 1/A mice and hybrid strains were transplanted into the oviducts of mammary tumor virus (MTV)-free females mated with vasectomized males. The offspring developed mammary tumors and transmitted MTV to foster-nursed mice. Intrauterine transmission of MTV was not seen when eggs of virus-free mice were transplanted into GRS 1/A mothers delivered by Cesarean section. C57BL and 020 females, foster-nursed on GRS 1/A hybrid mothers, transmitted MTV by their milk, but not by their eggs. It is concluded that information for the development of mammary tumors and production of MTV later in life is contained in the eggs of GR mice.

- 70-115 INTERFERENCE BETWEEN TWO STRAINS OF THE MOUSE MAMMARY TUMOR VIRUS IN THE GR MOUSE STRAIN. (E.) Van Der Gugten, A. (Netherlands Cancer Inst., Amsterdam) and P. Bentvelzen. Europ. J. Cancer 5(4):361-371, 1969.

The number of pregnancies required for development of typical neoplastic lesions of the GR-strain mammary gland (plaques) was considered a reliable measure of the carcinogenic stimulus, since these lesions developed only under the influence of pregnancy. A 2-pregnancy delay in the development of neoplastic lesions was seen when mice were inoc. with BALB/cfc3H mammary tumor-derived Bittner virus (BV; live, formalin-

or ether-treated) at age 4-7 wk. A 2-pregnancy delay was also seen in mice inoc. with GR mammary tumor-derived H₂O₂-treated Mühlbock virus (MV), but not with live virus. Both BV and MV were highly carcinogenic in BALB/c mice; reduced activity was seen after ether treatment and total loss of activity after heating or exposure to H₂O₂ or formalin. The results suggested that inoc. with BV or treated MV induced immunity to virus antigens which also attacked MV. It is suggested that antibodies or lymphocytes may attack virus-producing cells, with subsequent delay in the development of palpable tumors. Lymphocytes sensitized against BV, may also attack MV-producing mammary cells.

- 70-116 MAMMARY TUMOR VIRUS ACTIVITY IN MAMMARY TISSUES OF HORMONE-STIMULATED BALB/cfc3H/Crg1 MICE. (E.) Medina, D. (U. California Cancer Res. Genet. Lab., Berkeley), H. A. Bern, D. Brown and K. B. DeOme. Proc. Soc. Exp. Biol. Med. 131(1):180-183, 1969.

BALB/cfc3H primary duct, BALB/c HAN (hyperplastic alveolar nodules) outgrowth or BALB/c lobulo-alveolar tissue were transplanted into the inguinal gland-free fat pads of 3-wk.-old BALB/c female mice, free of mammary tumor virus (MTV). The mice were treated s.c. with pellets of estradiol (E) for 6 wk., followed by deoxycorticosterone acetate (DOCA) for 6 wk. Substantial MTV activity was seen after 3 wk. of hormonal stimulation (E + DOCA) in 6-wk.-old BALB/chC3H mice, but not until after 13 wk. in the intact virgin BALB/cfc3H mammary gland. After at least 3 wk. of E + DOCA admin., MTV activity was seen in both normal lobules and hyperplastic nodule outgrowths of BALB/c mice.

- 70-117 THYMIDINE PHOSPHATE POOLS AND DNA SYNTHESIS AFTER POLYOMA INFECTION OF MOUSE EMBRYO CELLS. (E.) Lindberg, U. (Karolinska Inst., Stockholm), B. A. Nordenskjöld, P. Reichard and L. Skoog. Cancer Res. 29(8):1498-1506, 1969.

When exposed to excess ³H-thymidine (T), mouse embryo cells contained 2'-deoxy-T5'-triphosphate (αTTP) as the predominant T compound. After 6 days, a relative increase in 2'-deoxy-T 5'-diphosphate and 2'-deoxy-T (TdR) incorporation and a decrease in the amount of T incorporation into DNA were noted, with no significant change in the total pool of T compounds. No differences in TdR phosphate pools were seen in dense and thin cell cultures. Stationary cultures infected with polyoma virus (PV) showed a dramatic increase in both DNA synthesis and the size of acid-soluble pools; the latter increase resulted mainly from an increase in the size of the dTTP pool. A 4-fold increase in ribonucleotide reductase activity was also seen. PV infection of thin, proliferating cultures caused a slight increase of TdR incorporation into DNA, but had no effect on the acid-soluble pools.

70-118 SIMIAN VIRUS 40 INFECTION OF UNINOCULATED AFRICAN GREEN MONKEYS (Cercopithecus aethiops) REVEALED BY REPEATED CELL PASSAGES. (E.) Orsi, E. V. (Seton Hall U., South Orange, N. J.), M. Franko, L. Rodriguez and H. T. Holden. Experientia 25(2):181-182, 1969.

After repeated rapid passage of presumably uninfected African green monkey kidney cultures, for 1 yr., evidence of SV40 was found in all cultures, including initially negative monolayers obtained from serologically negative monkeys. It is suggested that the African green monkey may be infected with SV40 in its natural environment or during shipping procedures. Cell division appeared to be necessary for the expression of the SV40 infection.

70-119 IN VITRO INTERACTION BETWEEN LYMPHOID CELLS AND FIBROBLAST CELLS OF NEWBORN HAMSTERS INFECTED WITH PAPOVAVIRUS SV40. (E.) Hamburg, V. (Acad. Med. Sci., Inst. Exp. Clin. Oncol., Moscow) S. Staroverova and L. E. Obukhova. Neoplasma (Bratisl.) 16(1):17-21, 1969.

Cell cultures were prepared from the skin of newborn Syrian hamsters 5-6 days after i.p. infection (at age 18-24 hr.) with SV40 (strain A-426, Rh-2); immune lymphoid cells were obtained from popliteal and inguinal nodes of adult hamsters 6 days after SV40 infection. When immune lymphocytes were added to the infected fibroblast culture, the cell monolayers were destroyed in 7/11 trials. It is concluded that this system may detect in vivo the new cell antigen induced by SV40 in vivo in tissues of newborn hamsters.

70-120 ABSENCE OF INFECTIOUS VIRUS FROM A LINE OF SV40-TRANSFORMED HUMAN LIVER CELLS. (E.) Khoury, G. and J. Van Der Noordaa (U. Amsterdam, Netherlands). Proc. Soc. Exp. Biol. Med. 131(1):297-300, 1969.

Primary cultures of human embryonic liver cells, infected with SV40 (strain VA 45-54), initially consisted mainly of spindle-shaped cells, without a CPE. Foci of rapidly dividing epithelioid cells were seen in 2/3 cultures after 4 wk. These cells (which did not occur in control cultures) showed morphological transformation and grew more rapidly than the surrounding fibroblasts. These transformed cells could be subcultured each wk., whereas control cultures could be subcultured only once. The T antigen was present in almost all nuclei of the tested cells from subcultures 6 and 14. No evidence of SV40 was seen in supernatants from subcultures 3-30; SV40 was also absent (despite heterokaryon formation), in cell fusion experiments in subcultures 9, 18 and 24.

70-121 CROSS-REACTING TSTAS IN ADENO 7 AND 12 TUMORS DEMONSTRATED BY ⁵¹Cr-CYTO-TOXICITY AND ISOGRAFT REJECTION TESTS. (E.) Ankerst, J. (U. Lund, Sweden) and H. O. Sjögren. Int. J. Cancer 4(3):279-287, 1969.

The colony inhibition and ⁵¹Cr-release (non-lymphoid target cells) methods were used to study complement-dependent cytotoxicity against adenovirus 7 (AV-7) and adenovirus 12 (AV-12) hamster tumor cells of antisera from mice (CBA, C3H/KL or (A/Sn X CBA)F₁ hybrid) hyper-immunized with 5-25 doses of X-irradiated (6000 r) AV-12 tumor cells. Hamster AV 7 tumor cells were immunogenic and induced an isograft immunity to AV-12 tumors, which resembled the immunity induced by AV-12 hamster and mouse tumor cells.

70-122 SEX-RELATED RESISTANCE IN HAMSTERS TO ADENOVIRUS-12 ONCOGENESIS. IV. GONADAL HORMONE INFLUENCES. (E.) Yohn, D. S. (Roswell Park Mem. Inst., Buffalo, N. Y.) and C. A. Funk. J. Nat. Cancer Inst. 43(1):133-139, 1969.

Adenovirus-12 (AV-12 0.1 ml s.c.) admin. to newborn Syrian hamsters, consistently induced a higher incidence of tumors in females than in males. The tumor incidence became the same for both sexes when animals were oophorectomized (oox.) or orchiectomized (orx.) at 1 wk. of age; the difference was not significant in animals orx. or oox. at age 3 wk. Oox. reduced the tumor incidence 10-18%, but orx. had a varied effect (7% decrease to 8% increase). Testosterone admin. (2 inj./wk. of 5 mg or less i.m. in normal animals; 0.5 mg/wk i.m. in oox. or orx. animals) had no effect on the tumor incidence. Estradiol (0.5 or 0.05 mg) increased the tumor incidence in oox. females and in intact and orx. males, but had no effect on the tumor incidence in intact females.

70-123 PATHOGENESIS OF ONCOGENIC SIMIAN ADENOVIRUSES. IV. THE HISTOPATHOLOGY AND ULTRASTRUCTURE OF INTRAPERITONEAL NEOPLASMS INDUCED BY SV20. (E.) Merkow, L. P. (U. Pittsburgh Sch. Med., Pa.), M. Slifkin, M. Pardo and N. P. Rapoza. Int. J. Cancer 4(4):455-464, 1969.

Newborn non-inbred Syrian hamsters were inj. i.p. with the Chin (A57) strain of SV20 and were examined for tumors at age 24-87 days. At age 30-60 days, about 80% developed hemorrhagic ascites and grossly palpable abdominal tumors, which comprised about 25% of the total body wt. (about 5 cm in diameter). Most tumors were pedunculated and/or adhered to visceral organs; they were cystic and necrotic and contained 2 types of giant tumor cells. The tumor cells were poorly differentiated, with oval, round or polygonal hyperchromatic nuclei, an increase in

dilated rough endoplasmic reticulum and a decrease in annulate lamellae. Cytoplasmic and nuclear virus-like particles (resembling SV20) were associated with the endoplasmic reticulum. Nuclear projections and unusual cytoplasmic bodies, with dense structures resembling the nucleoid of the virus particles, were also observed. Similar results were seen in SV20-infected LLC-MK2 cells in monolayer culture.

70-124 IN VITRO TRANSFORMATION BY AN AVIAN ADENOVIRUS (CELO). II. HAMSTER KIDNEY CELL CULTURES. (E.) Anderson, J. (U. Rhode Island, Kingston), V. J. Yates, V. Jasty and L. O. Mancini. J. Nat. Cancer Inst. 43(1):65-70, 1969.

Kidney cell cultures from 5-day-old hamsters were infected with plaque-purified CEL0 virus (Phelps strain). Virus production could not be demonstrated in the initial passages, but a virus-specific intranuclear T antigen was identified by immunofluorescence in almost all cells by passage 12. Tumors were induced after a latent period of 30-34 days in 5/7 1-wk.-old hamsters inoc. s.c. with 2.5×10^5 cells from passage 4; the latent period was 2 mo. in animals inoc. (as above) at age 4 wk. The tumors were circumscribed and firm, with some hemorrhagic areas; tumor growth was rapid (after several wk., the tumors were often approx.

the size of the animal). No metastases were seen.

70-125 RIBONUCLEOTIDE REDUCTASE ACTIVITY IN CELL-FREE EXTRACTS OF YABA POXVIRUS TUMOR AND NORMAL MONKEY TISSUES. (E.) Gordon, H. L. (Roswell Park Mem. Inst., Springville, N. Y.) and R. J. Fiel. Cancer Res. 29(7): 1350-1355, 1969.

The specific activity of ribonucleotide reductase (RNR) in cell-free extracts of Yaba poxvirus-induced tumors from monkeys (Macaca speciosa and Macaca mulatta) was double the activity seen in normal muscle tissue extracts, and 10-fold the activity in normal liver, spleen and kidney extracts. Activity of tumor RNR was increased by adenosine triphosphate (ATP), but did not require its presence. Enzyme activity was lost by dialysis of tumor extracts but not by dialysis of spleen extracts. The activity in extracts of Novikoff ascites hepatoma cells was higher than previously reported. It is suggested that a tumor-specific RNR is more active in the poxvirus tumor and differs from the cytidine diphosphate reductase present in the Novikoff ascites cells and in normal monkey spleen. RNR was inhibited by exogenous deoxy-ATP, deoxycytidine-5'-triphosphate, deoxyguanosine-5'-triphosphate and (to a lesser extent) deoxythymidine-5'-triphosphate.

70-126 EPIDEMIOLOGICAL STUDY OF LEUKEMIA IN JAPAN WITH SPECIAL REFERENCE TO THE PROBLEM OF TIME-SPACE CLUSTERING. (Jap.) Hirayama, T. (Nat. Cancer Ctr., Res. Inst., Tokyo). Acta Haemat. (Jap.) 31(5):737-747, 1968.

Several significant 1-yr. clusters of leukemia, resembling clusters seen for Japanese B encephalitis, scarlet fever, influenza and bacillary dysentery, were seen in Shiga and Nagano prefectures. Significant 1-yr. temporal clustering was also seen in Ehime and Kanagawa prefectures, with 2-yr. temporal clustering in Nagano prefecture. Time-space plotting of leukemia clusters seen in Okayama (1962-1966) and Shizuoka (1954-1965) showed a significantly shorter time interval between case pairs occurring within a short distance of each other (600-1250 meters) than between case pairs occurring at greater distances. No such relationship was seen between the time interval of birth and the distance interval of occurrence. Leukemia death rates/yr. in the 2-4 yr. age group in several regions of Japan showed striking fluctuations, of a magnitude resembling the occurrence rates for measles; the curves for Tokyo greatly resembled those seen for the neighboring prefectures (Kanagawa, Chiba and Saitama). A synthetic curve composed of 2 components, with modes at ages 0-1 and 2-4 yr. (reflecting predominantly pre- and postnatal influences, resp.), was established as a valid hypothetical model for cohort analysis of leukemia death rates in children in the U.S. (white and non-white) and Japan. The data were compatible with the theory of horizontal viral transmission, possibly co-existent with vertical transmission.

70-127 EPIDEMIOLOGY OF LUNG CANCER IN RELATIONSHIP TO PULMONARY TUBERCULOSIS. (It.) Aoki, K. (Nayoya U., Japan), J. Ipsen and S. C. Stein. Riv. Ist. Vac. Con. Pro. Antitub. 19(1):19-40, 1969.

The relationship between the risk of lung cancer and the presence of pulmonary tuberculosis (TB) was examined, using data from the U.S. (with particular reference to 1955-1964 data obtained in Philadelphia), Japan and Denmark (Copenhagen). The data studied are for males only. A significant excess risk of lung cancer was found among pts. with TB, especially with active TB. Mortality curves since 1930 in the U.S. (white and non-whites), Japan and Copenhagen showed a decrease in TB mortality and a concurrent increase in lung cancer mortality. When the mortality curves intersected, the increase in the lung cancer rates was postponed in proportion to the preceding level of TB mortality. A causative sequence between TB and cancer could not be established (in 1 pt. group, the 2 diseases were found in discordant sites in 77.9% of the pts.). A mathematical model (using U.S.

data for 1915-1960) was examined to test the hypothesis that a fraction of each birth cohort (approx. 6% of the male population at birth) is highly susceptible to both TB and lung cancer. If these persons escape or survive TB early in life, they have a high risk of developing lung cancer in later life.

70-128 TRENDS IN CANCER DEATH RATES IN THE LAST 50-60 YEARS, USING SWITZERLAND AS AN EXAMPLE. (Ger.) Gsell, O. (U. Basel Gen. Hosp., Switzerland). Z. Krebsforsch. 72(2): 197-210, 1969.

Age-standardized death rates/10,000 living persons for all carcinomas combined, decreased by 10% in males and 25% in females in Switzerland from 1910-1960. Rates for stomach carcinoma decreased markedly, with smaller decreases in the rates for carcinoma of the esophagus and colon (both sexes), and a sharp decrease in carcinoma of the cervix (females), during this time. Rates for carcinoma of the bronchus increased in both sexes, especially in males (a 24-fold increase was seen in males); death rates for carcinoma of the pancreas remained approx. stationary until 1940-1943, but doubled from that time to 1959-1962 (both sexes). The death rates for carcinoma of the prostate, ovary and female breast also increased. A comparison of these rates with the crude and standardized death rates for these and other tumors in 1952-1965, showed a continuance of the trends noted since 1910, except for decreased death rates for carcinoma of the ovary, breast and (after 1954) corpus uteri in females. In 1910, the 4 most frequent tumors seen in all age groups in males were g.i. carcinomas; after 1960, lung cancer was the most frequent tumor in males. A female preponderance was seen for gallbladder and thyroid cancer and a male preponderance (attributed to the effects of smoking) for cancer of the respiratory tract (mouth to bronchus) and bladder.

70-129 HEPATOMA IN THE AUTOPSY RECORDS OF THE ZURICH PATHOLOGICAL INSTITUTE FOR THE YEARS 1901-1966 (86,549 AUTOPSIES), WITH A METHOD FOR THE ESTIMATION OF EPIDEMIOLOGIC RELATIONSHIPS ON THE BASIS OF AUTOPSY STATISTICS. (Ger.) Fierz, L. (U. Zurich Path. Inst., Switzerland). Acta Hepatosplen. (Stuttgart) 16(6):383-398, 1969.

From 1901-1966, 283 hepatomas and 55 cholangiocarcinomas (250/283 and 50/55, resp., were histologically confirmed) were found among 86,549 autopsies in Zurich. During this time, the relative proportions of cholangiocarcinomas and hepatomas without cirrhosis remained relatively constant (about 0.07% and 0.045% of all autopsies, resp.), but the relative proportion

of hepatomas with cirrhosis rose from 0.04% of all autopsies (1901-1910) to 0.473% (1961-1966). Carcinomas were found in 10.5% of all autopsies (781/7414) in 1911-1920 and in 29.0% of all autopsies (4106/14,157) in 1961-1966; hepatomas comprised 1.28-1.44% of all carcinomas from 1911-1960 and 1.78% of all carcinomas in 1961-1966. A method for eliminating the influences of such factors as changing causes of death (with particular reference to infections) and changing age distribution of the autopsied population (with respect to the age at death in the total population) is described. After the application of this method, the data from this autopsy series showed a constant age-specific rate of hepatoma deaths during the period 1921-1966 in the 60-69 yr. age group (about 8% of all deaths), but a marked increase in the 50-59 and 70-79 yr. age groups (from 4% and 7.5% of all deaths, resp., in 1921-1930, to 8% and 12%, resp., in 1961-1966). This age-specific increase in hepatoma deaths was attributed to improved treatment of infections in pts. with cirrhosis. A mild increase of severe liver cirrhosis during the postwar period also had a certain role.

70-130 PATHOGENETIC SIGNIFICANCE OF CHOLELITHIASIS FOR THE DEVELOPMENT OF PRIMARY CARCINOMA OF THE GALLBLADDER. (Ger.) Heber, J. (Karl Marx U. Path. Inst., Leipzig, Germany). *Arch. Geschwulstforsch.* 33(4):356-374, 1969.

A 1962-1966 series from the author's Institute disclosed cholelithiasis (CL) in 3690/12,532 autopsied adults (29.44%) and primary gallbladder cancer (GBC) in 221/12,532 (1.76%). The male:female ratio was 1:0.97 in the total series. In the pts. with CL, GBC, GBC with CL (177/221 GBC pts.) and GBC without CL (44/221), a significant female preponderance was noted; female:male ratios were 1.89:1, 8.21:1, 9.4:1 and 5.3:1, resp. CL was noted in 81.22% of all females and 70.83% of all males with GBC; 97.7% of the pts. with CL + GBC were over 50 yr. old. The female preponderance in the total group with CL was greatest in the third and fourth decades. In the GBC group, the female preponderances in the total group and in the GBC + CL group were greatest in the sixth and eighth decades (female:male ratios were 23.5:1 and 13.3:1, resp., in the total GBC group, and 15.7:1 and 13.7:1, resp., in the GBC + CL group). It is suggested that processes involved in the pathogenesis of CL (especially hormone-dependent disturbances in cholesterol metabolism and the chronic cholecystitis associated with CL) may also affect the neoplastic transformation of the gallbladder epithelium. It is also suggested that the morphogenesis of GBC may be the same as that of scar carcinomas of other localizations.

70-131 HEPATOBLASTOMA IN INFANT SISTERS. (E.) Fraumeni, J. F., Jr. (NCI, Bethesda, Md.), P. J. Rosen, E. W. Hull,

R. F. Barth, S. R. Shapiro and J. F. O'Connor. *Cancer* 24(5):1086-1090, 1969.

Two sisters (the oldest and youngest of 4 children) died with hepatoblastoma in infancy (at age 11 wk. in 1/2 and 18 mo. in 1/2). No heritable or congenital disorders known to increase the risk of hepatoma were present. Serum α -fetoprotein was found repeatedly in the pt. who died at age 18 mo. The parents and 2 other siblings were clinically and serologically normal. No congenital abnormalities and no other cases of cancer in the family were reported. This is the first reported instance of familial hepatoblastoma.

70-132 CLINICO-PATHOLOGICAL STUDY ON MULTIPLE MYELOMA IN JAMAICA. (E.) Talerman, A. (Roy. Free Hosp., London). *Brit. J. Cancer* 23(2):285-293, 1969.

In 1957-1966 (inclusive), 101 cases of multiple myeloma and 3 of solitary plasmacytoma were reported in Jamaica (the av. population was about 1.5 million during this period). The group included 102 pts. of Negro or predominantly Negro origin, 1 white pt. and 1 Oriental pt. (about the same ethnic distribution as in all of Jamaica); the male:female ratio was 1.1:1. No evidence was found to suggest an earlier occurrence of multiple myeloma in the Negro population than in other groups. Amyloidosis and extramedullary involvement were seen at autopsy in a high proportion of these pts. The incidence of multiple myeloma is much higher in Jamaica than in African Negroes (no specific data are included).

70-133 FURTHER EVIDENCE OF SPACE-TIME CLUSTERING OF BURKITT'S LYMPHOMA PATIENTS IN THE WEST NILE DISTRICT OF UGANDA. (E.) Williams, E. H., P. Spit and M. C. Pike (Med. Res. Council Statistical Res. Unit, London). *Brit. J. Cancer* 23(2):235-246, 1969.

In 1966-1967 (inclusive), Burkitt's lymphoma (BL) was identified clinically or histologically in 29 residents (all children) of the West Nile district of Uganda, whose addresses were known. Analysis of these records confirmed the finding of time-space clustering, with the epidemic characteristic of "drift," in a larger group of BL pts. from the same district (previously described) who presented in 1961-1965. The largest cluster was seen in the Mount Wati area (1 case in 1961; 15 cases from July, 1964-November, 1967); 2 other clusters (4 and 2 cases, resp.) were also found. The total population of the West Nile District of Uganda in 1959 (excluding 1 region of over 5000 feet elevation) was about 337,500; in 1961-1967, BL was found in 70 residents of this district whose addresses were known. One large, sparsely populated area of the district (Vura and Madi Counties;

estimated population 21,500), however, has reported no known or suspected cases of BL in 17 yr. (the expected number was 4.5). No great differences were seen between this "blank area" and the remainder of the district, with respect to malaria rates or the results of large-scale mosquito catches and viral antibody studies.

70-134 KAPOSI'S SARCOMA IN MAINLAND TANZANIA: A REPORT OF 117 CASES. (E.) Slavin, G. (Muhimbili Hosp., Dar es Salaam, Tanzania), H. McD. Cameron and H. Singh. Brit. J. Cancer 23(2):349-357, 1969.

The 117 pts. with histologically diagnosed Kaposi's sarcoma seen in mainland (excluding Zanzibar and Pemba) from January, 1964-June 1966, included 8 children under 16; most pts. were 30-69 yr. old. Kaposi's sarcoma constituted 4% of all histologically diagnosed malignancies in Tanzania during 1964-1965. The male:female ratio was 12:1 in adults (who generally presented with skin lesions) and 3:1 in children (in whom the disease more often presented as lymph node enlargement). The male predominance (especially in adults) did not seem to result from case selection, and no direct evidence for a hormonal factor was found. Second primary tumors were found in 2/117 (Hodgkin's disease and squamous cell carcinoma of the leg in 1 pt. each).

70-135 CONTROL OF CERVIX CANCER IN WOMEN OF LOW INCOME IN A COMMUNITY. (E.) Christopherson, W. M. (U. Louisville Sch. Med., Louisville, Ky.) and J. E. Parker. Cancer 24(1):64-69, 1969.

From April 1, 1956-June 30, 1968, cervical smears were obtained from 37,209 women of a low-income level in Louisville (Jefferson County), Kentucky. The group was about equally divided between white and Negro women. Repeat screenings (total 51,063) were performed at return intervals of 1-12 yr. Initial cytological detection rates/1000 were 13.71 for all lesions combined, 3.79 for invasive squamous cell carcinoma and 4.41 for carcinoma in situ (0.00 and 0.14, resp., in women under 20; 4.65 and 5.40, resp., in women aged 20 yr. and over; 6.87 and 6.42, resp., in women aged 30 yr. and over; suggesting that screening of women under 20 is unrewarding). In the second and third screenings, the total detection rates/1000 fell to 10.51 and 10.35, resp.; in pts. examined 4 or more times the rate was 6.12/1000. The proportion of Stage I invasive carcinoma in the cytologically screened pts. (1956-1967) was 63.93%, compared to 35.71% in 1953-1956, before the cytological screening program was begun. It is believed that essentially all low-income women in Jefferson County have been screened at least once for cancer of the cervix.

70-136 RETICULAR CRITERIA OF BEGINNING INVASION OF SQUAMOUS CELL CARCINOMAS OF THE UTERINE CERVIX (STAGE I A). SQUAMOUS METAPLASIA OF THE CYLINDRICAL GLANDS OF THE CERVIX. (Fr.) Moricard, R. (Broca Hosp., Paris) and M. C. Marroum-Ghorra. C. R. Soc. Biol. (Paris) 162(12):2081-2085, 1968.

Nodules of squamous cell metaplasia of the cervical glands were histologically benign; the reticular basal membrane was continuous, and the mucin-containing cells were either localized on the surface of the squamous epithelium, or in the center of the metaplastic epithelial nodules. The metaplastic cells showed normal nuclei and few or no mitotic figures. In pts. with intraepithelial squamous cell carcinoma, the initial stage of invasion of the cervical glands was associated with intensive and abnormal proliferation of the tumor cells. Only after the intraglandular foci of carcinoma became vascularized was connective tissue invasion seen, beginning with localized dispersion of the reticulum fibers of the basal membrane and penetration of the tumor cells into the network of the dissociated fibers.

70-137 INFLUENCE OF SEX AND ESTRUS CYCLE ON CELL KINETICS IN THE EHRlich ASCITES TUMOR: AUTORADIOGRAPHIC STUDIES IN MICE. (Ger.) Adler, D. (U. Cologne Path. Inst., Germany) and K. J. Lennartz. Naturwissenschaften 56(11):565-566, 1969.

In female NMRI mice inoc. i.p. with a diploid strain of Ehrlich ascites carcinoma cells (5 days before inj. of ^{14}C - and/or ^3H -thymidine), the stage of the estrus cycle at which the cells were labeled had little or no influence on the cell growth kinetics. Diploid tumor cells from female mice showed a somewhat longer DNA-synthetic phase than tumor cells obtained from males, but little sex difference was seen with respect to the total generation time and the duration of the G2 + mitosis phase. Cell growth kinetics were also not influenced by the estrus cycle in female mice inoc. with hyper-tetraploid Ehrlich carcinoma cells.

70-138 A COMPARISON OF CELL PROLIFERATION PARAMETERS IN SOLID AND ASCITES EHRlich TUMORS. (E.) Tannock, I. F. (M. D. Anderson Hosp., Houston, Tex.). Cancer Res. 29(8):1527-1534, 1969.

In mice bearing ascites Ehrlich carcinoma, tumor growth was delayed for a short time immediately after inoc., followed by an increase in the doubling time from 12 hr. (2 days after i.p. tumor inoc.) to 6 days (10 days after inoc.). Studies of labeled mitotic figures showed an exponential growth curve during the first 3

days, with a median cell cycle time of 12 hr. By 6-9 days, all phases of the cell cycle had increased in duration; the median cell cycle time was 44 hr., the doubling time was 60 hr. and the mean S phase was 10 hr. In mice with solid tumors (inoc. s.c.), the doubling time increased from 2 days (0.1-g tumor) to a relatively constant value of about 10 days (0.5-2.0 g tumors). In these tumors, the median cell cycle time was 17 hr., with a median S period of 10 hr., a growth fraction of 0.8, and a cell loss factor of 90%. Solid tumors showed 60% necrosis, with a half-time of 36 hr. for resorption of necrotic material.

70-139 STIMULATION OF MAMMARY CARCINOMA CELL PROLIFERATION BY EPITHELIAL GROWTH FACTOR IN VITRO. (E.) Turkington, R. W. (Duke U. Med. Ctr., Durham, N. C.). Cancer Res. 29(7):1457-1458, 1969.

Highly purified epidermal growth factor (from submaxillary salivary glands of mice) was added (0.5 µg/ml) to explants of small, non-necrotic, spontaneous mammary adenocarcinoma from C3H/HeJ mice (cultured in medium 199). After an initial lag period of 8-12 hr., the rate of DNA synthesis in cultured cells was stimulated; at 48 hr., it was 4 times the control rate. This increase reflected an increase in the number of DNA-synthesizing cells. The rate of DNA synthesis/cell was not altered, although the rate of initiation of synthesis was increased.

70-140 SEPARATION OF DNA POLYMERASE FROM RAT LIVER AND HEPATOMAS. (E.) Ove, P. (Duke U. Med. Ctr., Durham, N. C.), O. E. Brown and J. Laszlo. Cancer Res. 29(8):1562-1567, 1969.

The pH 5.0 protein fraction was prepared from normal rat liver, regenerating rat liver and hepatoma tissue (9633, 5123-D and 7777, transplanted s.c. in male Buffalo strain rats) and its 5000 x g supernatant was applied to a Sephadex G-200 column. Two DNA polymerase peaks were eluted. The first peak had a 260 mµ/280 mµ ratio of about 1 and contained an enzyme preferring denatured DNA. Levels of this enzyme increased with the tumor growth rate. The second peak, with a 260 mµ/280 mµ ratio of about

1.7, contained an enzyme preferring native DNA; this peak accounted for the majority of enzyme activity in normal and regenerating liver. The first peak, was also elevated in several slowly growing renal tumors and in human chronic lymphocytic leukemic cells, in which the rate of thymidine incorporation into DNA was normal or less than normal. It is suggested that there are at least 2 distinct DNA polymerase enzymes.

70-141 HISTOGENETIC BEHAVIOR OF TUMORS. I. MORPHOLOGIC VARIATION IN VITRO AND IN VIVO OF TWO RELATED HUMAN CARCINOMA CELL LINES. (E.) Auersperg, N. (U. British Columbia, Vancouver, Canada). J. Nat. Cancer Inst. 43(1):151-173, 1969.

In vitro growth patterns of the C-4 I and C-4 II cell lines of human squamous cell carcinoma of the cervix (originating from the same biopsy) were reproduced in the patterns of invasion in the hamster cheek pouch. The C-4 cells grew as proliferating, tight masses, in vivo, while the C-4 II cells formed small nodules which infiltrated the connective tissue. In tissue culture the 2 lines reacted differently to crowding; the C-4 I cells grew in compact epithelial colonies, while the C-4 II cells formed expanding colonies.

70-142 HISTOGENETIC BEHAVIOR OF TUMORS. II. ROLES OF CELLULAR AND ENVIRONMENTAL FACTORS IN THE IN VITRO GROWTH OF CARCINOMA CELLS. (E.) Auersperg, N. (U. British Columbia, Vancouver, Canada). J. Nat. Cancer Inst. 43(1):175-190, 1969.

The related cell lines C-4 I and C-4 II (from a human squamous cell carcinoma of the cervix) did not differ in their responses to divalent-cation depletion or trypsin treatment. Colloidal iron staining was more extensive after aldehyde fixation than after Carnoy's fixation in both cell lines. Ferritin penetrated into the intercellular spaces of stationary colonies in both cell lines. Differences in stratification and colony morphology were apparently related to differences in the relative strength of intercellular cohesion and adhesiveness to substrata. Differences in adhesiveness were correlated with ultrastructural cell surface characteristics and with the differential roles of extracellular cations and proteins.

70-143 OTHER MALIGNANT NEOPLASMS ASSOCIATED WITH CARCINOMA OF THE THYROID: THYROID CARCINOMA MULTIPLEX. (E.) Wyse, E. P., C. S. Hill (U. Texas M. D. Anderson Hosp., Houston), M. L. Ibanez and R. L. Clark. Cancer 24(4): 701-708, 1969.

Of 687 pts. with thyroid carcinoma seen during a 24-yr. period, 117 (17%) showed another primary tumor. In 65/117, the other primary was diagnosed simultaneously with or after the diagnosis of the thyroid tumor. The risk of developing a second primary tumor after the diagnosis of thyroid cancer was 1.4%/yr. This group included 8 pts. with 3 primary tumors each, and 1 pt. with 4. The relative incidence of multiple primary tumors in pts. with the various histological types of thyroid tumors was almost identical with the incidence of the histological tumor types themselves. Nonthyroid primary tumors originated in the head and neck in 26/117, the chest in 11/117, the abdomen in 15/117, the endocrine glands in 6/117, the reticuloendothelial system in 7/117, the skin in 31/117 and the pelvic organs in 16/117.

70-144 PRIMARY ADENOCARCINOMA OF THE RECTO-VAGINAL SEPTUM ARISING FROM ENDOMETRIOSIS. REPORT OF A CASE. (E.) Young, E. E. (U. California Sch. Med., San Francisco) and C. N. Gamble. Cancer 24(3):597-601, 1969.

Pathological changes occurring during a 3-yr. course of malignant transformation of endometriosis of the rectovaginal septum to a well-differentiated adenocarcinoma (adenocanthoma) in a 47-yr.-old woman are described. The pt. had undergone hysterectomy with bilateral oophorectomy, followed by admin. of a preparation containing conjugated estrogen + methyltestosterone + ascorbic acid (to prevent menopausal symptoms), 11 yr. before this mass developed, but the hysterectomy specimen showed chronic salpingitis with oophoritis and multiple ovarian abscesses, without signs of endometriosis or cancer. This pt. brings to 6 the number of reported cases of primary adenocarcinoma of the rectovaginal septum arising in a area of endometriosis.

70-145 DERMATOGLYPHIC DEFECTS IN CHILDREN WITH LEUKAEMIA. (E.) Menser, M. A. (Roy. Alexandra Hosp. Child., Sydney, Australia) and S. G. Purvis-Smith. Lancet 1(7605):1076-1078, 1969.

Sydney lines were seen in 20% of 25 children with leukemia and in 7% of 100 age- and race-matched controls; simian lines were seen in 16% and 6%, resp. Frequencies of Sydney lines and of simian or Sydney lines, but not of simian lines alone, were significantly higher in the

children with leukemia than in the controls. The incidence of various digital patterns in leukemic pts. and controls were: whorls (25.2% and 22.8%, resp.); ulnar loops (60.4% and 67.7%, resp.); radial loops (7.6% and 5.7%, resp.); and arches (6.8% and 3.8%, resp.). No difference between the two groups was seen in the incidence of interdigital patterns. The mean elevation of the axial triradius was 20.0% in the pts. with leukemia and 21.5% in the controls. It is suggested that the Sydney line may be a significant marker for an underlying lesion.

70-146 EFFECT OF ANTILYMPHOCYTE SERUM ON PARAMETERS OF TUMOR GROWTH IN A SYNGENEIC TUMOR-HOST SYSTEM. (E.) Fisher, B. (U. Pittsburgh Sch. Med., Pa.), O. Soliman and E. R. Fisher. Proc. Soc. Exp. Biol. Med. 131(1):16-18, 1969.

Anti-mouse lymphocyte serum (ALS) was prepared in rabbits from lymph node and thymus tissue of C3H mice. When C3HeB/FeJ mice were inj. intraperitoneally with a suspension of 100,000 C3H tumor cells, followed by 14-21 days of treatment with either ALS or normal rabbit serum (NRS; 0.25 mg/day i.p.) after tumor inoc., liver metastases developed in mice receiving ALS, but not in controls. When fragments of C3H tumors were implanted s.c. in C3HeB/FeJ mice treated with ALS or NRS, tumors developed after 30 days in 100% of the ALS-treated mice, but in only 50% of the animals admin. NRS. In the ALS group, the tumors appeared earlier, grew to larger size, and occasionally formed liver and lung metastases.

70-147 STUDIES OF TUMOUR INVASION IN ORGAN CULTURE. I. EFFECTS OF BASIC POLYMERS AND DYES ON INVASION AND DISSEMINATION. (E.) Yarnell, M. M. (Roy. Cancer Hosp. Chester Beatty Res. Inst., London) and E. J. Ambrose. Europ. J. Cancer 5(3):253-263, 1969.

The effects of toluidine blue (TB) and poly-L-lysine (pL) were studied in organ cultures of fetal mouse heart maintained for 5 days, after addition of known numbers of BHK21 Py cells (the medium consisted of agar, modified Eagle's medium, horse serum and embryo extract). Addition of pL (up to 150 µg/ml) caused no cell damage in the presence of serum, but pL penetrated the cells (resulting in cell death) in the absence of serum; the pL molecule was apparently preferentially adsorbed on the serum molecule. TB was progressively lethal above 1 µg/ml. Nonlethal concn. of TB caused polarization; the BHK21Py cells were seen lying in sheaves (as non-transformed BHK21 cells do in monolayer culture), with the long axes parallel; the cells and nuclei were flat and elongated. Pretreatment of invading BHK21Py cells with pL at 75 µg/ml

caused a reduction in invasion; this was also attributed to adsorption of the pL molecule, resulting in a decrease in cell motility. The results failed to support the hypothesis that the degree of contact inhibition is regulated by the presence of charged molecules at the surface, and that the reduction of this charge will prevent invasion in vitro.

70-148 STUDIES OF TUMOUR INVASION IN ORGAN CULTURE. II. EFFECTS OF ENZYME TREATMENT. (E.) Yarnell, M. M. (Roy. Cancer Hosp. Chester Beatty Res. Inst., London) and E. J. Ambrose. Europ. J. Cancer 5(3):265-269, 1969.

Neuraminidase (NA; 10 IU/ml) and trypsin (T 0.02-1.0%) were used to remove surface materials from BHK21Py cells invading into fetal mouse heart explants in culture. NA had no adverse effects on either explants or invading cells. Exposure to 1% T (for 5 days) resulted in complete digestion of the explant and the invading cells; at 0.2% T, 100% digestion of the explants and 67% digestion of invading cells was seen. At 0.1%, T had no adverse effect on the invading cells and caused slight digestion of the explants. Addition of T-pretreated (0.1%) Py cells was associated with death of 18% of the explants. Neither NA-treated nor untreated Py cells invaded during the first 48 hr. after deposition on the explant; after 48 hr., less invasion was found with the pretreated cells than with untreated cells until day 5, when the degree of invasion was similar with both cell cultures. Exposure to all concn. of T was followed by increased invasion; at 0.1% T, 74% of the cultures showed increased invasion, while pretreatment with 0.1% T caused increased invasion in only 15% of the cultures. Polarized cells were not seen in either NA- or T-treated cultures, but gamma cells were frequent. The nature of invasion was not altered by NA or T treatment. The effects of NA were related to its effect on sialic acid on the cell surface; the effects of T were related to nutrition and resulted mainly from enzymatic lysis of the explant.

70-149 EVOLUTION OF CELL-MEDIATED IMMUNITY IN MICE BEARING AN ANTIGENIC TUMOR. INFLUENCE OF TUMOR GROWTH AND SURGICAL REMOVAL. (E.) Barski, G. (Gustave Roussy Inst, Villejuif, France) and J. K. Youn. J. Nat. Cancer Inst. 43(1):111-121, 1969.

Peritoneal cells (PC) from preimmunized BALB/c mice suppressed almost completely T5 target cell colony growth in vitro; inhibition was seen 126 days after the last inj. In 1-2 mo.-old BALB/c mice inoc. s.c. with 2×10^6 T5 tumor cells, tumors appeared in 10 days; PC obtained from these animals at the beginning of tumor growth had slightly inhibited the growth of T5 cells in vitro. However, PC from animals with large

tumors did not inhibit T5 growth, but tended to enhance growth. When the tumors were removed 17 days after inoc., PC from these mice had no significant suppressing effect on T5 cell growth in vitro, but PC obtained 12 days or more after surgery were highly suppressive. This effect lasted at least 56 days after surgery. In animals receiving another inoc. (7 and 14 days after surgery) of X-irradiated cells of the original tumor (stored frozen), recovery of the inhibitory action of PC was accelerated.

70-150 PROPAGATION AND MICROMORPHOLOGY OF A HUMAN LEUKOCYTE CULTURE (M-1) AND OF CULTURES DERIVED FROM ITS TRANSPLANTATION IN HAMSTERS. (E.) Chandra, S. (Chas. Pfizer & Co., Inc., John L. Smith Mem. Cancer Res., Maywood, N. J.), F. T. Buscheck, C. Garon and R. A. Manaker. Cancer Res. 29(10):1821-1828, 1969.

The M-1 cell line was established from peripheral WBC of an adult with acute lymphocytic leukemia. In Eagle's MEM medium supplemented with human serum, the cells grew as a suspension culture in glass vessels and as a monolayer culture in plastic containers; in MEM and 199 medium containing fetal calf serum, the cells grew as monolayers in any vessel. The number of giant cells varied with different media. Similar morphology was seen in both M-1 and M-1-like cells, (cell cultures derived from tumors produced in conditioned hamsters by M-1 cells). A paucity of Golgi apparatus was seen in M-1 cells grown in 2 of the media used, while hypertrophy of the Golgi apparatus was seen in a third medium. Neither the M-1 nor the M-1-like cells contained any virus-like particles, but degenerating cells sometimes contained aggregates of bodies (45 mμ in diameter), bound by a single smooth membrane.

70-151 MORPHOLOGIC AND SEROLOGIC STUDIES OF TRANSPLANTED HUMAN LEUKOCYTE CULTURE (M-1) CELLS IN LABORATORY ANIMALS. (E.) Chandra, S. (Chas. Pfizer & Co., Inc., John L. Smith Mem. Cancer Res., Maywood, N. J.), D. E. Brown, P. Aldenderfer, C. Garon, F. T. Buscheck and R. A. Manaker. Cancer Res. 29(10):1829-1839, 1969.

In 24-hr.-old golden hamsters, s.c. or i.p. inj. of M-1 human leukemic cell cultures induced no tumors, but intracranial inj. of M-1 cells, followed by cortisone conditioning (3 mg s.c. at the time of tumor inoc., then 1 mg every 4 days), resulted in a large s.c. tumor on the skull (at the site of the tumor cell inj.) in 1 animal. This tumor was subpassaged (s.c.) 4 times in conditioned hamsters, but not in conditioned mice. Cell cultures derived from these tumors were more tumorigenic than the original M-1 cell culture. These tumor cells were not transformed hamster cells; the human origin of the M-1 cells and cells of 2 subpassages

was demonstrated by mixed agglutination tests. The presence of aggregates of round cells in the hamster tumors suggested *in vivo* transplantation of the lymphoblastic and epithelial-like cells of the M-1 culture. The nuclei of many tumor cells showed many small (28 mμ) dense granules, possibly reflecting a host response to the tumor.

70-152 SPONTANEOUS INTERSTITIAL AND SERTOLI CELL TUMORS OF A TESTIS IN A C3H MOUSE. (E.) Franks, L. M. (Imperial Cancer Res. Fund, London). Cancer Res. 28(1):125-127, 1968.

In a 16-mo.-old male C3H Heston stock mouse with a spontaneous mammary tumor, the testes appeared grossly normal but the prostate and seminal vesicles were atrophic. Two tumors were found in 1 testis. The larger tumor was of tubular adenomatous structure, with closely packed clear cells with hyperchromic nuclei, and resembled a Sertoli cell tumor. The smaller tumor was a typical interstitial cell tumor with sheets of granular, polygonal cells resembling normal Leydig cells. Where the 2 tumors were in contact, cords of interstitial tumor cells were found between the tubular elements of the Sertoli cell tumor. It is suggested that the Sertoli cell tumor was estrogen-producing.

70-153 ULTRASTRUCTURAL OBSERVATIONS ON AN UNIDENTIFIED CELL TYPE FOUND IN EPIDERMAL TUMORS OF FLOUNDERS. (E.) Brooks, R. E. (U. Oregon Med. Sch., Portland), G. E. McArn and S. R. Wellings. J. Nat. Cancer Inst. 43(1):97-109, 1969.

An unknown cell type was found in the dermis and epidermis of angioepithelial nodules of the flounder. Cells found in the dermis were characterized by a large nucleolus and numerous small, discrete nuclear chromatin clumps. The outer nuclear membrane was well separated from the inner membrane. Paired cells were common; many cells had an external cell coat about 500 Å thick. Cells in the epidermis were similar but considerably larger and contained increased numbers of all cytoplasmic elements. Some cells had an extracellular coat about half as thick as that seen in dermal cells.

70-154 THROMBOCYTOPENIA, A PRELYMPHOID LEUKEMIC SIGN IN AKR MICE. (E.) Brodsky, I. (Hahnemann Med. Coll., Philadelphia, Pa.). Nature (London) 223(5202):198-199, 1969.

lean platelet counts in 3-wk.-old mice were 502,500 in 30 AKR mice and 983,400 in 30 BALB/c mice. Bone marrow imprints from both groups were similar; in AKR mice, the bone marrows showed megakaryocytes with no evidence of leukemic infiltration. In the AKR mice, the platelet count increased with age, then decreased with the onset of leukemia; this phenomenon paralleled

that seen in BALB/c mice infected with high dilutions (10^{-3}) of Rauscher leukemia virus. The AKR mice recovered from the initial thrombocytopenia in 13-28 wk., with a median survival time of 38.0 wk; a similar recovery was seen in infected BALB/c mice at 6-10 wk., with a median survival time of 21.1 wk.

70-155 DECREASE TO COMPLETE LOSS OF ABILITY TO BIND ESTRADIOL BY A SOLUBLE MACROMOLECULAR FRACTION OF C3H MAMMARY TUMORS. (E.) Puca, G. A. (Inst. Gen. Pathol., Messina, Italy) and F. Bresciani. Europ. J. Cancer 3(6):475-479, 1968.

The 105,000 x g supernatant fraction was prepared from mammary tumors or normal mammary glands obtained from 8-14-mo.-old multiparous, oophorectomized C3H/HeJ female mice, or normal mammary glands exposed for 1 hr. to ^3H -labeled estradiol (E ; 10^{-2} μg) at 4°C, then chromatographed on a Sephadex G-100 column. Several 280 mμ peaks were eluted. Using normal mammary gland extracts, the first such peak contained macromolecules excluded from the internal phase of the gel, and was significantly able to bind E non-covalently. This capability was minimal or absent in mammary tumor extracts. It is suggested that these estradiolophilic macromolecules may serve to inhibit cell proliferation.

70-156 CHROMOSOME PATTERN OF BONE MARROW FIBROBLASTS IN PATIENTS WITH CHRONIC GRANULOCYTIC LEUKAEMIA. (E.) Maniatis, A. K. (Tufts U. Sch. Med., Medford, Mass.), S. Amsel, W. J. Mitus and N. Coleman. Nature (London) 222(5200):1278-1279, 1969.

Bone marrow was collected from 7 pts. with chronic granulocytic leukemia and cultured in glass bottles (at 37°C for 10 days). Cells attached to the glass were detached, trypsinized and prepared for chromosomal analysis; direct bone marrow aspirates were also examined. The Philadelphia chromosome (Ph^1) was seen in 88 direct bone marrow metaphase preparations from 7/7 pts. Metaphases from fibroblasts in the bone marrow cultures showed marked aneuploidy with a majority of hypodiploid forms and normal chromosomes in group G, but no Ph^1 chromosomes were seen in any of the 28 metaphases observed. It is concluded that the fibroblast-like cells from bone marrow cultures in these pts. were not derived from granulocytic, erythrocytic or megakaryocytic elements or their common precursor cell (the hemocytoblast). The insult leading to deletion of the G-2 chromosome apparently occurred at the level of the hemocytoblast, not at the level of the undifferentiated mesenchymal cell.

70-157 CHRONIC MYELOCYTIC LEUKEMIA. CHROMOSOME STUDIES OF A PATIENT AND HIS NONLEUKEMIC IDENTICAL TWIN. (E.) Bauke, J.

(Res. Ctr. Clin., Ulm/Donau, Germany). Cancer 24(3):643-651, 1969.

A Ph¹-positive karyotype was found in both peripheral blood cells and bone marrow cells of a man with chronic granulocytic leukemia, but not in his monozygotic (probability greater than 99.8%) twin, who had only normal diploid cells in both tissues when examined, 8.5 yr. after the diagnosis of leukemia in the pt.

70-158 CHROMOSOMES IN BURKITT LYMPHOMAS. I. SERIAL STUDIES IN A CASE WITH BILATERAL TUMORS SHOWING DIFFERENT CHROMOSOMAL STEMLINES. (E.) Gripenberg, U. (Kenyatta Nat. Hosp., Nairobi, Kenya), A. Levan and P. Clifford. Int. J. Cancer 4(3):334-349, 1969.

In a pt. with Burkitt's lymphoma involving both sides of the face (as well as cervical lymph node metastases), cells from the tumor on 1 side showed a normal diploid karyotype, whereas cells from the tumor on the other side showed 46 chromosomes with several markers (predominantly M2 and MC, with a smaller number of MB and MD markers; M2 was later replaced by M1 through translocation of the distal segment). During treatment (irradiated autochthonous tumor cells, DL-sarcosine, vincristine sulfate, cytosine arabinoside and methotrexate, during the 3 mo. before death), marked chromosomal breakage was seen in the tumor cells. A cell line, established in the early stages from the tumor with the abnormal karyotype, showed many polyploid cells (the result of endoreduplication) and all of the marker chromosomes except M1.

70-159 GENE CONTROL OF NEOPLASIA. I. GENOTYPIC MOSAICISM IN NORMAL AND PRE-NEOPLASTIC MAMMARY GLANDS OF ALLOPHENIC MICE. (E.) Mintz, B. (Inst. Cancer Res., Philadelphia, Pa.) and G. Slemmer. J. Nat. Cancer Inst. 43(1):87-95, 1969.

Normal mammary glands, hyperplastic nodules and 1 mammary adenocarcinoma from allophenic female mice (C3Hf <-> C57BL/6; 11 mo. or 1 yr. old) were studied for genotypic composition. Cells of both strains were found in the normal mammary glands, suggesting that epithelium is derived from at least 2 cell clones. Hyperplastic nodules also showed cells from both strains, but graft outgrowths from these nodules showed clear strain-specific growth patterns. The mammary adenocarcinoma had a similar genotypic composition. It is suggested, from these strain-specific growth patterns, that hyperplastic nodules were a mixture of premalignant C3Hf and normal C57 cells.

70-160 CHROMOSOMAL ANALYSIS OF TUMORS DERIVED FROM MOUSE CELLS AFTER NEOPLASTIC CONVERSION IN VITRO IN VARIOUS SERUM-SUPPLEMENTED MEDIA. (E.) Parshad, R. and K. K. Sanford (NCI, Bethesda, Md.). J. Nat. Cancer Inst. 43(1):71-76, 1969.

Tumors studied were derived from implants into C3Hf/HeN mice of cell lines 5449 and 5508. The number of chromosomes in the tumor cells varied widely, but were sometimes characteristic of the sublines in vitro. No common pattern of chromosomal composition was noted in the different tumors.

- Adams, D. H. 103
 Adler, D. 137
 Aldenderfer, P. 151
 Alfred, L. J. 36
 Ambrose, E. J. 147,148
 Ames, W. R. 23
 Amsel, S. 156
 Anderson, J. 124
 Ankerst, J. 121
 Aoki, K. 127
 Auersperg, N. 141,142
- Baker, M. S. 36
 Bard, D. S. 43
 Barr, L. M. 104
 Barron, N. A. 53
 Barry, E. J. 3
 Barski, G. 149
 Barth, R. F. 131
 Bartus, B. 61
 Bates, R. R. 31,46
 Bather, R. 110
 Bauke, J. 157
 Belman, S. 4
 Ben, T. 85
 Bentvelzen, P. 115
 Berenblum, I. 58
 Bergs, V. V. 101
 Berman, L. 108
 Bern, H. A. 116
 Bockman, D. E. 76
 Bonser, G. M. 7
 Bresciani, F. 155
 Brodsky, I. 154
 Brilliantine, L. 33
 Brooks, R. E. 153
 Brown, D. 116
 Brown, D. E. 151
 Brown, E. V. 63
 Brown, H. D. 55
 Brown, O. E. 140
 Brown, R. R. 70
 Bryan, G. T. 71
 Bubenik, J. 109
 Burch, P. R. J. 13
 Burney, S. W. 70
 Burr, K. 33
 Buscheck, F. T. 150,151
 Bushar, H. F. 87
- Cameron, H. McD. 134
 Canter, H. Y. 73
 Caprio, G. 77
 Carbone, P. P. 62
 Carter, R. L. 38,39,53
 Chandra, S. 150,151
 Chany, C. 111
 Chattopadhyay, S. K. 55
 Chen, L. 58
 Chirigos, M. A. 97
 Chouroulinkov, I. 45
 Christopherson, W. M. 135
- Chuatz, J.-C. 108
 Clark, R. L. 143
 Clarke, M. A. 40
 Clarke, W. J. 26
 Clemens, J. A. 54
 Clifford, P. 158
 Coffin, A. 33
 Coleman, N. 156
 Colnaghi, M. I. 77
 Commins, B. T. 32
 Cook, M. K. 91
 Counts, W. B. 46
 Coune, A. 44
- Dabrowski, S. 90
 Dawson, P. J. 106
 DeGowin, E. L. 30
 Deichmann, W. B. 69
 Della Porta, G. 77
 DeOme, K. B. 116
 Dingman, C. W. 46
 DiPaolo, J. A. 36
 Donovan, P. J. 36
 Dulbecco, R. 10
 Dunlop, W. R. 85
 Dutton, A. M. 23
- Elashoff, R. M. 21
 Elmer, I. 49
 Engle, C. G. 52
 Engstrom, G. W. 79
 Epstein, S. M. 61
- Fadda, G. 109
 Falk, H. L. 31
 Farber, E. 61
 Fiala, S. 12
 Fiel, R. J. 125
 Field, E. J. 103
 Fieldsteel, A. H. 106
 Fierz, L. 129
 Fishbein, L. 31
 Fisher, B. 146
 Fisher, E. R. 146
 Flaks, A. 60
 Flaks, B. 60,64
 Franko, M. 118
 Franks, L. M. 152
 Fraumeni, J. F., Jr. 131
 Friedell, G. H. 70
 Funk, C. A. 122
- Gallien-Lartigue, O. 99
 Gamble, C. N. 144
 Garon, C. 150,151
 Gart, J. J. 31
 Gelboin, H. V. 46
 Ghelelovitch, S. 27
 Ghosh, A. K. 75
 Gibbs, G. W. 32
- Gitlin, D. 62
 Goldfeder, A. 75
 Goldman, M. 87
 Goodheart, C. R. 9
 Gordon, H. L. 125
 Griffin, W. 97
 Gripenberg, U. 158
 Groupé, V. 52
 Gsell, O. 128
 Guérin, M. 45
 Gunvén, P. 108
 Gutmann, H. R. 3
- Halliday, W. J. 51
 Hamann, W. 34
 Hamburg, V. 119
 Hammond, W. G. 43
 Haran-Ghera, N. 58
 Harnden, D. 83
 Hart, E. R. 31
 Hays, E. F. 102
 Heber, J. 130
 Heimann, R. 44
 Hempelmann, L. H. 23
 Hertz, R. 2
 Heuson, J. C. 44
 Hill, C. S. 143
 Hirayama, T. 126
 Hoffmann, D. 35
 Holden, H. T. 118
 Horne, M. K. 84
 Hoshino, T. 19
 Hosokawa, M. 100
 Howard, E. B. 26
 Huebner, R. J. 8,94
 Hull, E. W. 62,131
- Ibanez, M. L. 143
 Ikawa, Y. 98
 Imamura, N. 20
 Innes, J. R. M. 31
 Ipsen, J. 127
 Ito, T. 20
 Ito, Y. 88
 Izard, C. 45
- Jänisch, W. 17
 Jasty, V. 124
 Jensen, M. M. 96
 Jobst, K. 37
 Joyce, G. 103
- Kato, R. 81
 Kawakami, T. G. 105
 Kawase, A. 20
 Kawazoe, Y. 78
 Kelly, M. G. 62
 Khoury, G. 120
 Kimura, I. 88
 Kinzel, V. 47

- Kipp, W. H. 63
 Kirsten, W. H. 107
 Kitabatake, T. 18
 Klein, E. 11, 108
 Klein, M. 31
 Kobayashi, H. 100
 Kodama, T. 100
 Korol, W. 93
 Krishna Murthy, A. S. 72
 Kurahara, C. 106
 Kurita, Y. 88
- Lagerlöf, B. 29
 Laszlo, J. 140
 Lazar, P. 45
 Lemon, H. M. 1
 Lennartz, K. J. 137
 Levan, A. 158
 Libermann, C. 45
 Liechty, R. D. 30
 Lijinsky, W. 66
 Lindberg, U. 117
 Lingeman, C. H. 14
 Linker-Israeli, M. 59
 Ludwig, F. C. 21
 Lukes, R. J. 33
 Lynch, H. T. 15
- Malejka-Giganti, D. 3
 Manaker, R. A. 150, 151
 Mancini, L. O. 124
 Maniatis, A. K. 156
 Marchant, J. 41, 42
 Mark, J. 112
 Marhold, J. 65
 Marroum-Ghorra, M. C. 136
 Martin, H. 25
 Matka, M. 65
 Maurer, R. 47
 McArn, G. E. 153
 Medina, D. 116
 Meites, J. 54
 Menser, M. A. 145
 Menye, P. A. 24
 Merkow, L. P. 61, 123
 Metchell, E. Z. 85
 Mettler, F. A., Jr. 23
 Mickey, M. R. 56
 Miller, D. G. 16
 Mintz, B. 159
 Mirand, A. G. 95
 Mirand, E. A. 95
 Mirvish, S. S. 58
 Mishima, Y. 82
 Mitchell, I. 31
 Mitus, W. J. 156
 Moody, J. A. 64
 Moon, R. C. 57
 Moricard, R. 136
 Moscovici, C. 92
 Mukai, F. 4
 Munn, R. J. 105
 Murthy, H. S. R. 80
- Nomura, S. 85
 Nordenskjöld, B. A. 117
 Noronha, F. 104
 Noyes, W. F. 50
- Obukhova, L. E. 119
 O'Connor, J. F. 131
 Odaka, T. 98
 Oehlert, W. 34
 O'Gara, R. W. 62
 Omori, Y. 81
 Onoda, K. 81
 Orsi, E. V. 118
 Osato, T. 88
 Ove, P. 140
- Pallotta, A. J. 31
 Pamukcu, A. M. 68
 Pardo, M. 61, 123
 Parker, J. E. 135
 Parker, J. W. 33
 Parmiani, G. 77
 Parshad, R. 160
 Patel, A. B. 55
 Pearson, J. 97
 Pennington, S. N. 55
 Pereira, M. F. 6
 Peters, J. 31
 Peto, R. 22
 Petrucelli, L. 31
 Pifer, J. W. 23
 Pike, M. C. 133
 Pilch, Y. H. 43
 Pinkel, D. 90
 Pipalová, J. 65
 Pope, J. H. 84
 Post, J. E. 104
 Prehn, R. T. 28
 Price, J. M. 68, 70
 Puca, G. A. 155
 Pugh, R. P. 55
 Purvis-Smith, S. G. 145
- Radomski, J. L. 69
 Rambo, O. N. 21
 Rambousek, V. 65
 Ragab, A. H. 89
 Raj, H. G. 80
 Rapoza, N. P. 123
 Reichard, P. 117
 Reisher, J. I. 87
 Rhim, J. S. 94
 Rickard, C. G. 104
 Robbe-Maridor, F. 111
 Rodriguez, L. 118
 Roe, F. J. C. 38, 53
 Rosen, P. J. 131
 Ross, A. 83
 Ross, A. E. 66
 Rush, J. D. 105
 Russfield, A. B. 72
- Saito, T. 48
 Sanford, K. K. 160
 Schilli, W. 34
 Schmid, F. A. 49
 Schreiber, D. 17
 Scott, W. 84
 Sendo, F. 100
 Serafino, X. 24
 Shapiro, S. R. 131
 Shimkin, M. B. 73
 Singh, H. 134
 Sjögren, H. O. 121
 Skoog, L. 117
 Slavín, G. 134
 Slemmer, G. 159
 Slifkin, M. 123
 Smida, J. 113
 Smidová, V. 113
 Smith, J. W. 90
 Smith, R. E. 92
 Soliman, O. 146
 Somers, K. D. 107
 Spiro, R. H. 25
 Spit, P. 133
 Spjut, H. J. 55
 Spratt, J. S. 55
 Stamler, F. W. 30
 Staroverova, S. 119
 Stein, S. C. 127
 Steiner, J. 33
 Stern, E. 56
 Stewart, S. E. 85
 Strong, E. 25
 Stutman, O. 76
 Süß, R. 47
 Swart, B. E. 86
- Takahashi, H. 29
 Takahashi, M. 82
 Takanaka, A. 81
 Takayama, S. 67
 Takeichi, N. 100
 Takizawa, K. 98
 Talterman, A. 132
 Tambourin, P. 99
 Tannock, I. F. 138
 Tarnowski, G. S. 49
 Theilen, G. H. 105
 Ting, R. C. 94
 Todaro, G. J. 8
 Toth, B. 74
 Toyooka, E. T. 23
 Trainin, N. 59
 Troll, W. 4
 Turano, A. 109
 Turkington, R. W. 139
 Turner, W. 97
- Uehara, N. 78
 Ulland, B. M. 31
- Valerio, M. G. 31
 Van Der Gugten, A. 115

Van Der Noordaa, J. 120
Venkatasubramanian, T. A. 80
Vietti, T. J. 89
Viswanathan, L. 80
Volm, M. 47
Vredevoe, D. L. 102

Whang, J. J. 85
Williams, E. H. 133
Wortham, J. S. 46
Wright, B. S. 93
Wright, J. K. 22
Wynder, E. L. 35
Wyse, E. P. 143

Yates, V. J. 124
Yohn, D. S. 122
Yokoro, K. 20
Youn, J. K. 149
Young, B. G. 86
Young, E. E. 144

Webb, M. 51
Wellings, S. R. 153
Welsch, C. W. 54
Wendling, F. 99

Yamasaki, T. 20
Yang, J. 110
Yarnell, M. M. 147, 148

Zajdela, F. 99
Zasynka, A. T. 5
Zeilmaker, G. H. 114

SUBJECT INDEX

- ACETYLAMINOFLUORENE (See N-2-Fluorenylacetamide)
- ACTIDIONE (See under Antitumor agents)
- AFLATOXIN(S)
 analysis, method: 79
 biosynthesis, *Aspergillus* cell-free preparations: 80
 effect on liver drug-metabolizing enzymes, animal: 81
- AFLATOXIN B-1
 effect on serum proteins, monkey: 62
- AMIDES, AROMATIC
 mechanism of action, review: 3
- ANDROGENS (See under Hormones)
- ANTITUMOR AGENTS
 actinomycin D
 effect on
 DNA and dimethylbenzanthracene carcinogenesis, mouse skin: 46
 mouse hepatitis-sarcoma virus system *in vitro*: 111
 cycloheximide (Actidione), effect on skin carcinogenesis, mouse: 47
 effect on Friend leukemia virus infection, mouse: 96
 6-mercaptopurine, effect on radiation leukemogenesis, mouse: 21
 puromycin, effect on mouse hepatitis-mouse sarcoma virus system *in vitro*: 111
 synthetic copolymer, effect on viral leukemia, mouse: 97
- ASBESTOS
 contamination by polyethylene containers: 32
- AZOBENZENE, 4'-DIMETHYLAMINO-
 derivatives, structure-activity relationship, liver tumors, rat: 63
 metabolism, bile, rat: 65
- AZOBENZENE, 3'-METHYL-4-DIMETHYLAMINO
 effect on serum proteins, monkey: 62
- AZOXYMETHANOL, METHYL- (See Cycasin aglycone)
- BENZANTHRACENE
 effect on dimethylbenzanthracene cytotoxicity, hamster embryonic cells: 36
- BENZANTHRACENE, 1:2,5:6-DI-
 effect on Rous virus tumors, chick: 52
- BENZANTHRACENE, 7,12-DIMETHYL-
 cytotoxicity, effect of benzanthracene, hamster embryonic cells: 36
 effect on
 DNA, hamster embryonic cells: 36
 Rous virus tumors, chick: 52
 epidermal tumors, oophorectomized rat: 44
 lymphoma, hamster: 74
 mammary tumors
 effect of
 contraceptive, rat: 56
 hypothalamic and amygdaloid lesions, rat: 54
 reproductive history, rat: 57
 oophorectomized rat: 44
 protein binding, effect of cycloheximide, mouse skin: 47
 s.c. tumors
 primate: 50
- BENZANTHRACENE, 7,12-DIMETHYL- (Contd.)
 strain difference, mouse: 49
 skin tumors
 effect of
 actinomycin D, mouse: 46
 cycloheximide, mouse: 47
 tobacco smoke or tar, mouse: 35,45
 thymoma, ultrastructure, mouse: 76
- 3,4-BENZOPYRENE
 effect on Rous virus tumors, chick: 52
 protein binding, effect of cycloheximide, mouse skin: 47
 s.c. sarcomas, primate: 50
 uptake, oral mucosa, hamster: 34
- BILIARY TRACT
 dimethylaminoazobenzene metabolism, rat: 65
- BIPHENYL, 3:2'-DIMETHYL-4-AMINO-
 mammary tumors, LDH isozymes, rat: 55
- BLADDER CARCINOGENESIS
 bracken fern (*Pteris aquilina*), rat: 68
 β -naphthylamine, dog or human: 4
 tryptophan metabolites, review: 5
- BLADDER NEOPLASMS
 urinary tryptophan metabolites, Boston or Wisconsin: 70
- BONE NEOPLASMS
 induction, ^{90}Sr , swine: 26
- BRACKEN FERN (See under Plants and plant extracts)
- BRAIN NEOPLASMS
 induction, animal, review (book): 17
 methylnitrosourea-induced, DNA and histone content, rat: 37
- BREAST NEOPLASMS (See Mammary neoplasms, human)
- BRONCHUS NEOPLASMS
 methylnitrosourea-induced, DNA and histone content, rat: 37
- CARCINOGENESIS (general and unspecified)
 mechanism, theory, review: 12
 RNA viruses, mechanism, review: 8
- CARCINOGENESIS, CHEMICAL (See also under Radiation carcinogenesis and Viral carcinogenesis)
 CNS, animal, review (book): 17
 occupational, review: 6
- CARCINOGENS, CHEMICAL
 screening, dog and rodent, review: 7
- CELL GROWTH KINETICS
 ascites or solid Ehrlich carcinoma: 138
 cervix cancer cell lines (C-4 I and II)
 hamster: 141
in vitro: 141,142
 effect of
 basic polymers and dyes, transformed cells: 147
 enzymes, transformed cells: 148
 estrus cycle, mouse tumor: 137
 mouse mammary tumors, effect of epithelial growth factor *in vitro*: 139
 rat liver or hepatoma, DNA polymerase activity: 140
 Stage IA (intraepithelial) cervix cancer: 136
- CERVIX UTERI NEOPLASMS
 cell lines (C-4 I and II)

- CERVIX UTERI NEOPLASMS (Contd.)
 growth kinetics
 hamster: 141
 In vitro: 141,142
 epidemiology, Kentucky (Louisville): 135
 growth kinetics, intraepithelial tumors: 136
- CHROMOSOMES (See also Genetics, cellular)
 genotypic mosaicism, mammary tumors, allophenic mice: 159
 markers
 Burkitt lymphoma: 158
 transformed human cell lines, herpes-type virus: 88
 Ph¹, chronic granulocytic leukemia: 156,157
 Rous virus-induced mouse sarcoma: 112
 tumors from transformed cells, mouse: 160
 urethan-induced lymphosarcoma, mouse: 77
- COCARCINOGENESIS
 tobacco smoke, skin, mouse: 35
- CONNECTIVE TISSUE NEOPLASMS
 Kaposi's sarcoma, epidemiology, Tanzania (mainland): 134
- CORTICOSTEROIDS (See under Hormones)
- CROTON OIL PHORBOL ESTERS
 cocarcinogenesis, effect of cycloheximide, mouse skin: 47
- CYCASIN AGLYCONES (methylazoxymethanol)
 effect on serum proteins, monkey: 62
- DIETHYLSTILBESTROL
 kidney tumors, enzymes, hamster: 72
 testis tumors, mouse: 73
- DISEASE TRANSMISSION
 Rauscher leukemia virus, mouse: 95
- ENDOCRINE ABLATION
 adrenalectomy, effect on Friend leukemia virus infection, mouse: 96
 orchiectomy or oophorectomy, effect on methylcholanthrene s.c. tumors, mouse: 41
- ENVIRONMENTAL FACTORS
 urbanization, bladder cancer, tryptophan metabolism, Boston or Wisconsin: 70
- ENZYMES
 dehydrogenases, estrogen-induced kidney tumor, hamster: 72
 DNA polymerase, relationship to growth rate, rat liver or hepatoma: 140
 lactate dehydrogenase isozymes, mammary tumor, rat: 55
 microsomal, effect of aflatoxin, animal liver: 81
 ribonucleotide reductase, Yaba virus-induced monkey tumors: 125
- EPIDEMIOLOGY
 all tumors, Switzerland: 128
 breast cancer
 abnormal estrogen balance, review: 1
 estrogen + progestagen contraceptives, review: 2
 irradiated postpartum mastitis, New York (upstate): 23
 bladder cancer, urinary tryptophan metabolites, Boston or Wisconsin: 70
- EPIDEMIOLOGY (Contd.)
 Burkitt's lymphoma, Uganda (West Nile District), clustering: 133
 cervix cancer, Kentucky (Louisville): 135
 cholangiocarcinoma of liver, Switzerland (Zurich): 129
 gallbladder cancer, East Germany, cholelithiasis, sex difference: 130
 hepatoma with/without cirrhosis, Switzerland (Zurich): 129
 Kaposi's sarcoma, Tanzania (mainland): 134
 leukemia
 children, Japan, time-space clusters and virus diseases: 126
 diagnostic or therapeutic radiation, Japan: 18
 radiation exposure, Japan (Hiroshima-Nagasaki): 19
¹³¹I-treated thyrotoxicosis, Japan: 19
 lung cancer
 risk, pulmonary TB, males: 127
 Switzerland, smoking: 128
 myeloma, Jamaica: 132
 review: 14
- ESOPHAGUS NEOPLASMS
 induction, nitrosopiperidine, mouse: 67
- ESTROGENS (See under Hormones)
- ESTRUS CYCLE
 effect on cell growth kinetics, mouse tumor: 137
- N-2-FLUORENYLACETAMIDE
 effect on
 Rous virus tumors, chick: 52
 serum proteins, monkey: 62
 ultrastructure, pancreatic exocrine cells, rat: 64
 liver tumors
 mechanism of action, rat, review: 3
 ultrastructure, rat: 61
- N,N'-2,7-FLUORENYLENEBISACETAMIDE
 effect on serum proteins, monkey: 62
- FUNGICIDES AND HERBICIDES
 liver and other tumors, mouse: 31
- GALLBLADDER NEOPLASMS
 epidemiology, East Germany, cholelithiasis, sex difference: 130
- GASTROINTESTINAL CARCINOGENESIS
 bracken fern (*Pteris aquilina*), rat: 68
 nitrosopiperidine, mouse: 67
- GENETICS, ANIMAL
 dimethylbenzanthracene sensitivity, strain difference, mouse: 49
 preleukemic thrombocytopenia, AKR mouse strain: 154
- GENETICS, CELLULAR (See also Chromosomes)
 mosaicism, mammary tumors, allophenic mice: 159
 theory of malignant transformation, review: 13
- GENETICS, HUMAN
 dermatoglyphic defects, children, leukemia: 145

GENETICS, HUMAN (Contd.)

- hepatoblastoma, siblings (infants): 131
- skin cancer, review: 15

GENITAL NEOPLASMS, FEMALE

- adenocarcinoma of rectovaginal septum, transformed from endometriosis: 144

HEMATOPOIESIS

- effect of radiation and leukemia virus, mouse: 99

- preleukemic thrombocytopenia, AKR mice: 154

HORMONES (See also under Endocrine ablation)

- androgens, effect on adenovirus-12 tumors, hamster: 122

contraceptives

- effect on chemical mammary carcinogenesis, rat: 56

- mammary and genital cancer, animal and human, review: 2

- corticosteroids, effect on mammary tumor virus, mouse: 116

estrogens (See also Diethylstilbestrol)

- balance, breast cancer, review: 1
- binding loss, mouse mammary tumor: 155
- effect on adenovirus-12 tumors, hamster: 122

- mammary tumor virus, mouse: 116

- synthesis, Sertoli cell tumor (testis), mouse with mammary tumor: 152

HYDRAZINE COMPOUNDS

- leukemia and lung or skin tumors, structure-activity relationship, mouse: 58

HYDROXYLAMINE, 1- OR 2-NAPHTHYL-

- s.c. tumors, mouse: 69

HYPOTHALAMUS

- injury, effect of induced mammary tumors, rat: 54

IMMUNE SERUM

- antilymphocyte serum, effect on syngeneic tumor-host system, mouse: 146

effect on

- Harvey sarcoma virus carcinogenesis, mouse or rat: 109

- viral lymphoma, mouse: 102

IMMUNITY

cellular

- hamster tumors from human leukemic WBC culture (M-1): 151

- mouse sarcoma virus-transformed cells: 108

- SV40 antigens, detection method: 119

- T5 mouse tumor: 149

- tumor-specific surface antigens, review: 11

- Harvey sarcoma virus, mouse or rat: 109

- human leukemia and lymphoma, review: 16

- lymphoid cells, effect on urethan lung tumors, mouse: 59

- methylcholanthrene-induced tumors, mouse: 42,43,51

- serum herpes-type virus antibodies, leukemia and lymphoma, detection methods: 87

IMMUNOSUPPRESSIVE AGENTS

- effect on viral lymphoma, mouse: 102

INDENE, 1-(4-DIMETHYLAMINOBENZAL)-

- mammary and s.c. tumors, rat: 53

INJURIES (See also Scar tissue)

- phagedenic ulcer of leg, malignant transformation, Senegal: 24

INTERFERON

- induction (synthetic copolymer), effect on viral leukemia, mouse: 97

KIDNEY CARCINOGENESIS

- diethylstilbestrol, enzymes, hamster: 72

- methylnitrosourea, DNA and histone content, rat: 37

KIDNEY NEOPLASMS

- Wilms' tumor (child), transformed culture, papovavirus-like particles: 90

LACTATION

- effect on dimethylbenzanthracene mammary carcinogenesis, rat: 57

LEUKEMIA, EXPERIMENTAL (See also Virus, leukemia/lymphoma)

- Moloney (viral), effect of rat virus (RV-13 or 9HV-B), rat: 101

- spontaneous, preleukemic thrombocytopenia, AKR mice: 154

- thymic lymphocytic, virus particles, cat: 104

LEUKEMIA, HUMAN

- cell-free extract, transformed embryonic cell lines, chromosome markers and herpes-type virus: 88

cell lines

- hamster tumors: 150,151

- herpes-type virus: 84,86

- child, infectious mononucleosis, Epstein-Barr antibodies: 89

- chronic granulocytic, Ph¹ chromosome: 156,157

- chronic lymphocytic, immunity, review: 16

epidemiology

- children, Japan, time-space clusters and virus diseases: 126

- dermatoglyphic defects, children: 145

- screening for virus particles: 83

- serum herpes-type virus antibodies, detection methods: 87

LEUKEMOGENESIS, EXPERIMENTAL (See also under Radiation leukemogenesis)

dimethylbenzanthracene

- hamster: 74

- oophorectomized rat: 44

- thymoma, ultrastructure, mouse: 76

- mouse leukemia virus, radiation effects, rat: 20

- pesticides, mouse: 31

urethan

- lymphosarcoma, chromosomes, mouse: 77

- related compounds, structure-activity relationship, mouse: 58

- X-ray, virus-like particles, mouse: 75

LEUKOSIS, AVIAN (See also Marek's disease)

- BA1 strain A virus, properties of non-transforming subgroups: 92

LIVER

DNA and RNA, effect of nitrosamines, rat: 66
microsomal enzymes, effect of aflatoxin,
animal: 81

LIVER CARCINOGENESIS

diethylnitrosamine, serum α -fetoprotein,
monkey: 62
dimethylaminoazobenzene derivatives, structure-
activity relationship, rat: 63
fluorenylacetamide
mechanism, rat, review: 3
ultrastructure, rat: 61
pesticides, mouse: 31

LIVER DISEASES

cirrhosis, with hepatoma, epidemiology,
Switzerland (Zurich): 129

LIVER NEOPLASMS

cholangiocarcinoma or hepatoma, with/without
cirrhosis, epidemiology, Switzerland
(Zurich): 129
hepatoblastoma, siblings (infants): 131
rat hepatoma, DNA polymerase activity and
growth rate: 140

LUNG CARCINOGENESIS

methylcholanthrene, mouse: 60
nitrosopiperidine, mouse: 67
urethan
effect of lymphoid cells, mouse: 59
related compounds, structure-activity
relationship, mouse: 58

LUNG DISEASES

tuberculosis, lung cancer risk, males: 127

LUNG NEOPLASMS

risk, pulmonary TB, males: 127

LYMPHOMA, MALIGNANT, EXPERIMENTAL

dimethylbenzanthracene-induced, hamster: 74
Friend virus-induced
pathology, disappearance of virus, mouse:
98

rat, pathology: 100
reticulum cell sarcoma, loss of virus
in vitro, mouse: 106

⁹⁰Sr induction, swine: 26

LYMPHOMA, MALIGNANT, HUMAN

Burkitt's
cell lines, herpes-type virus: 84,86
interferon production: 86
epidemiology, Uganda (West Nile District),
clustering: 133
karyotype: 158
serum herpes-type virus antibodies,
detection methods: 87
Hodgkin's disease, virus isolation and pro-
perties: 85
immunity, review: 16

MALIGNANT TRANSFORMATION

cholelithiasis to gallbladder cancer, sex
difference: 130
endometriosis of rectovaginal septum to adeno-
acanthoma: 144
mechanism, theory, review: 12,13
phagedenic ulcer of leg to carcinoma, Africa
(Senegal): 24
SV40 or polyoma virus, mechanism, review: 10

MAMMARY CARCINOGENESIS, EXPERIMENTAL (See also
Virus, mammary tumor)

abnormal estrogen balance, rat, review: 1
1-(4-dimethylaminobenzal)indene, rat: 53
dimethylaminobiphenyl, LDH isozymes, rat: 55
dimethylbenzanthracene
effect of
contraceptive, rat: 56
hypothalamic and amygdaloid lesions, rat:
54
reproductive history, rat: 57
oophorectomized rat: 44

estrogens or estrogen + progestagen combina-
tions, review: 2

MAMMARY CARCINOGENESIS, HUMAN

radiotherapy for mastitis, New York (upstate):
23

MAMMARY NEOPLASMS, EXPERIMENTAL

genotypic mosaicism, allophenic mice: 159
loss of estradiol binding, mouse: 155
male mouse, estrogen-producing Sertoli cell +
interstitial cell tumor of testis: 152
transplanted, effect of radiation or mammary
tumor virus, mouse: 28

MAMMARY NEOPLASMS, HUMAN

epidemiology
abnormal estrogen balance, review: 1
estrogen + progestagen contraceptives,
review: 2
irradiated postpartum mastitis, upstate
New York: 23

MAREK'S DISEASE (See also Leukosis, avian)

CAL-1 strain, properties of virus: 91

MELANOMA, MALIGNANT

hamster, virus-like particles: 82

METHYLAZOXYMETHANOL (See Cycasin aglycone)

3-METHYLCHOLANTHRENE

effect on Rous virus tumors, chick: 52
lung tumors, mouse: 60
s.c. sarcoma
effect of

endocrine ablation, mouse: 41
thymus graft, mouse: 41,42

immunity, mouse: 43,51

ultrastructure, mouse: 40

skin tumors, ultrastructure, mouse: 48

MYELOMA AND RELATED DISEASES

epidemiology
Jamaica: 132
review: 14

α -NAPHTHYLAMINE

metabolism, dog: 69

β -NAPHTHYLAMINE

metabolism, dog: 69

proximal bladder carcinogens, dog or human: 4

NEOPLASMS, EXPERIMENTAL

angioepithelial tumor of flounder, pathology:
153

C3H tumor (mouse), effect of antilymphocyte
serum, syngeneic tumor-host system: 146

Ehrlich carcinoma (mouse), ascites or solid,
growth patterns: 137,138

from transformed cells, karyotype, mouse: 160

T5 tumor (mouse), cell-mediated immunity: 149

tumor-specific surface antigens, review: 11

NEOPLASMS, HUMAN

double or multiple primary, with thyroid cancer: 143

epidemiology, Switzerland: 128

tumor-specific surface antigens, review: 11

4-NITROQUINOLINE 1-OXIDE

tritium labeling: 78

NITROSAMINE COMPOUNDS

effect on DNA and RNA, rat liver: 66

NITROSAMINE, DIETHYL-

hepatoma, serum α -fetoprotein, monkey: 62

1-NITROSOPIPERIDINE

effect on serum proteins, monkey: 62

g.i. and lung tumors, mouse: 67

N-NITROSO-2,2,4-TRIMETHYL-1,2-DIHYDROQUINOLINE (rubber additive)

s.c. sarcoma, rat: 39

N-NITROSOUREA, N-METHYL-

lung, CNS and other tumors, DNA and histone content, rat: 37

NUCLEIC ACIDS, DNA

carcinogen interactions, hamster embryonic cells: 36

effect of

dimethylbenzanthracene and actinomycin, mouse skin: 46

epithelial growth factor, mouse mammary tumors *in vitro*: 139

nitrosamines, rat: 66

methylnitrosourea-induced tumors, rat: 37

polymerase, relation to growth rate, rat liver or hepatoma: 140

polyoma virus

infected mouse embryo cells: 117

transformed cells, review: 10

radiation-induced mouse thymoma: 29

SV40-transformed cells, review: 10

NUCLEIC ACIDS, RNA

effect of nitrosamines, rat: 66

viral, determinants of cancer, review: 8

NUCLEOSIDES AND NUCLEOTIDES

ribonucleotide reductase, Yaba virus-induced monkey tumors: 125

OCCUPATIONAL DISEASES

chemical or radiation carcinogenesis, review: 6

PANCREAS

exocrine, effect of fluorenylacetamide, ultra-structure, rat: 64

PESTICIDES

liver and other tumors, mouse: 31

PHORBOL ESTERS (See under Croton oil)

PLANTS AND PLANT EXTRACTS

bracken fern (*Pteris aquilina*), g.i. and bladder tumors, rat: 68

herbicides, liver and other tumors, mouse: 31

legumes, mitogenic properties, normal human lymphocytes: 33

PLASTICS

polyethylene

containers, contamination of asbestos samples: 32

PLASTICS (Contd.)

s.c. sarcoma, rat: 38

PREGNANCY

effect on dimethylbenzanthracene mammary carcinogenesis, rat: 57

PROTEINS

benzpyrene or dimethylbenzanthracene binding, effect of cycloheximide, mouse skin: 47

histones, methylnitrosourea-induced tumors, rat: 37

serum α -fetoprotein, induced hepatoma, monkey: 62

RADIATION CARCINOGENESIS

Drosophila: 27

¹³¹I, thyroid, human: 30

mathematical models: 22

occupational, review: 6

postpartum mastitis radiotherapy, New York (upstate): 23

skin, head and neck, human: 25

⁹⁰Sr, bone, swine: 26

RADIATION EFFECTS

Friend virus leukemia, mouse: 99

postponement of radiation leukemogenesis, mouse: 21

promotion of viral leukemia, rat: 20

transplanted mammary tumor, mouse: 28

RADIATION LEUKEMOGENESIS, EXPERIMENTAL

DNA replication, mouse thymoma: 29

effect of radiation or 6-mercaptopurine, mouse: 21

⁹⁰Sr, bone, swine: 26

RADIATION LEUKEMOGENESIS, HUMAN

diagnostic or therapeutic radiation, Japan: 18

¹³¹I, Japan: 19

Japan, Hiroshima-Nagasaki: 19

RADIOACTIVE ISOTOPES AND ELEMENTS

¹³¹I, thyroid tumor, human: 30

⁹⁰Sr, leukemia, swine: 26

RESPIRATORY NEOPLASMS

epidemiology, Switzerland, smoking: 128

RUBBER ADDITIVES

nitrosoquinoline derivative, s.c. sarcoma, rat: 39

SALIVARY GLAND

submaxillary, epithelial growth factor, effect on mouse mammary tumors *in vitro*: 139

SCAR TISSUE (See also under Injury)

phagedenic ulcer of leg, malignant transformation, Senegal: 24

SEX

difference

adenovirus-12 tumor incidence, hamster: 122

gallbladder cancer with cholelithiasis, East Germany: 130

growth kinetics of Ehrlich ascites carcinoma mouse: 137

SKIN

oral mucosa, benzpyrene uptake, hamster: 34

SKIN CARCINOGENESIS

dimethylbenzanthracene

SKIN CARCINOGENESIS (Contd.)

- + croton oil, effect of cycloheximide, mouse: 47
 - effect of actinomycin D, mouse: 46
 - oophorectomized rat: 44
 - + tobacco smoke or tar, mouse: 35
 - methylcholanthrene, ultrastructure, mouse: 48
 - radialtion, head and neck, human: 25
 - s.c. tumors
 - benzpyrene, primate: 50
 - 1-(4-dimethylaminobenzal)indene, rat: 53
 - dimethylbenzanthracene
 - primate: 50
 - strain difference, mouse: 49
 - methylcholanthrene
 - effect of endocrine ablation, mouse: 41
 - thymus graft, mouse: 41,42
 - host immunity, mouse: 42,51
 - ultrastructure, mouse: 40
 - nitrosoquinoline derivative (rubber additive), rat: 39
 - polyethylene, rat: 38
 - tobacco tar + dimethylbenzanthracene, mouse: 45
 - urethan and related compounds, structure-activity relationship, mouse: 58
- SKIN NEOPLASMS
- heredity, review: 15
 - phagedenic ulcer of leg, malignant transformation, Senegal: 24
- STOMACH NEOPLASMS
- induction, nitrosopiperidine, mouse: 67
- STRESS
- effect on Friend leukemia virus infection, mouse: 96

TESTIS NEOPLASMS

- interstitial cell
 - diethylstilbestrol induction, mouse: 73
 - mixed (Sertoli cell), possible estrogen synthesis, mouse with mammary tumor: 152

THYROID NEOPLASMS

- frequency of double or multiple primary tumors: 143
- induction, ¹³¹I (thyrotoxicosis), human: 30
- methylnitrosourea-induced, DNA and histone content, rat: 37

UTERINE NEOPLASMS

- radiation-induced, DNA replication, mouse: 29

UTERUS

- graft
 - effect on methylcholanthrene s.c. tumors, mouse: 41
 - tumor immunity, induced sarcoma, mouse: 42

TOBACCO

- tars, skin tumors, mouse: 45

TOBACCO SMOKE

- cocarcinogenesis, skin, mouse: 35

TOBACCO SMOKING

- respiratory cancer, Switzerland: 128

TRAUMA (See Injuries)

TRYPTOPHAN METABOLITES

- bladder cancer
 - Boston or Wisconsin, urbanization: 70

TRYPTOPHAN METABOLITES (Contd.)

- review: 5

URETHAN

- lung tumors, effect of lymphoid cells, mouse: 59
- lymphoma
 - chromosomes, mouse: 77
 - virus-like particles, mouse: 75
- related compounds, leukemia and skin or lung tumors, structure-activity relationship, mouse: 58

VIRAL CARCINOGENESIS

- RNA viruses, mechanism, review: 8

VIRUS

- diseases, time-space leukemia clusters, children, Japan: 126
- lactate dehydrogenase-elevating (Riley agent), induction of CNS symptoms, mouse: 103
- mouse hepatitis, replication, effect of mouse sarcoma virus *in vitro*: 111
- morphology, hamster melanoma: 82
- RNA-containing, determinants of cancer, review: 8
- RV-13 or 9HV-B rat virus, effect on Moloney (mouse) leukemia virus infection, rat: 101
- SV5 (simian), virus resembling, isolation and properties, Hodgkin's disease: 85
- Type A particles
 - dimethylbenzanthracene-induced thymoma, mouse: 76
 - urethan + X-ray-induced thymic lymphoma, mouse: 75

VIRUS, ADENO-

- CELO (avian), hamster tumors: 124
- SV20 (simian), hamster tumors, pathology: 123
- type 7, cross-reactivity, mouse or hamster tumor: 121
- type 12
 - cross-reactivity, mouse or hamster tumor: 121
 - tumor incidence, sex difference, hamster: 122
- animal tumor viruses, classification, review: 9

VIRUS, HERPES

- Type 1, infection (genital), cervix cancer, review: 9

VIRUS, HERPES-TYPE

- Epstein-Barr (human)
 - acute leukemia with infectious mononucleosis, child: 89
 - cell lines, interferon production: 86
 - review: 9
 - serum antibodies, leukemia and lymphoma, detection methods: 87
- human
 - embryonic cell lines transformed by leukemic cell extract, chromosomes: 88
 - isolation, Hodgkin's disease: 85
 - properties, leukemic WBC (QIMR-WIL) or Burkitt lymphoma cells (QIMR-GOR): 84
 - Marek's disease (chicken), CAL-1 strain, properties: 91

VIRUS, LEUKEMIA/LYMPHOMA

BAI strain A avian myeloblastosis, properties of non-transforming subgroups: 92

cat leukemia

properties: 104

Type C particles, propagation: 105

Friend (mouse)

effect of interferon-inducing synthetic copolymer: 97

infection, effect of stress: 96

radiation effects: 99

pathology of rat tumors: 100

tumor pathology and disappearance of virus, mouse: 98,106

Gross (mouse)

effect of immune sera or immunosuppressive agents, mouse: 102

radiation promotion, rat: 20

Moloney (mouse)

infection, effect of rat virus (RV-13 or 9HV-B), rat: 101

transformed cells, antigenic characterization: 108

mouse erythroblastosis, interference with

MSV-K sarcoma virus: 107

Rauscher (mouse)

effect of interferon-inducing synthetic copolymer: 97

G8-6 strain, propagation, human embryonic cells: 93

HL-67-4 plasma virus, propagation, human embryonic cells: 93

transformation, hamster embryo cells: 94

transmission: 95

screening, leukemic or normal blood or bone marrow, human: 83

VIRUS, MAMMARY TUMOR

milk agent (mouse), effect on transplanted mammary tumor: 28

mouse

VIRUS, MAMMARY TUMOR (Contd.)

Bittner and Muhlbock strains, interference: 115

hormone effects in vivo: 116

transmission: 114

VIRUS, PAPOVA (papilloma-polyoma-vacuolating)

particles resembling, Wilms' tumor (child), transformed culture: 90

polyoma

effect on DNA, mouse embryo cells: 117

transformation, mechanism, review: 10

SV40

cellular antigens, detection method: 119

infection, pathogenesis, monkey: 118

transformation, human embryonic cells: 120

mechanism, review: 10

VIRUS, POX

Yaba (monkey), monkey tumors, ribonucleotide reductase activity: 125

VIRUS, SARCOMA

Harvey (mouse)

effect of immune sera, mouse or rat: 109

transformed cells, antigenic characterization: 108

Moloney (mouse)

effect on mouse hepatitis virus replication in vitro: 111

transformed cells, antigenic characterization: 108

effect of myo-inositol: 110

MSV-K (mouse), interference by mouse erythroblastosis virus: 107

Rous (chicken)

effect of carcinogens, chick: 52

inactivation, heat or ether: 113

mouse sarcoma, karyotype: 112

XANTHURENIC ACID 8-METHYL ETHER

metabolism, mouse: 71

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FEBRUARY 1970

Abstract Nos. 161-350



CARCINOGENESIS ABSTRACTS

National Cancer Institute

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE • National Institutes of Health

CARCINOGENESIS ABSTRACTS

Volume 8, Number 2
February, 1970

Abstract Numbers
161-350

CONTENTS

	<u>Page</u>
Review	33
Physical Carcinogenesis	34
Chemical Carcinogenesis	35
Viral Carcinogenesis	54
Epidemiology and Biometry	67
Miscellaneous	70
Author Index	i
Subject Index	iv

Prepared by Scientific Literature Corporation
Philadelphia, Pennsylvania 19103

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Persuant to a Contract with the Public Health Service
U.S. Department of Health, Education and Welfare
PH43-70-2036

Use of funds for printing this publication approved
by the Director of the Bureau of the Budget on July 25, 1967.

FOREWORD

The National Cancer Institute, in response to Congressional Interest and desire for a national program of cooperative research in cancer, is establishing a means whereby information in the field of carcinogenesis will be coordinated and made available. The information to be included will be obtained from the National Cancer Institute, other governmental agencies, and non-governmental research institutions.

The issuing of Carcinogenesis Abstracts under the auspices of the National Cancer Institute will provide a central source for current abstracting of the carcinogenesis literature being published throughout the world. This will help facilitate an integrated and cooperative program of investigation in this area. The growing number of publications in the area of carcinogenesis makes imperative the availability of an appropriate abstracting service so that investigators may be apprised of progress with a minimum of delay. It is our desire to provide the investigator with a readily systematized compilation of the published work.

Carcinogenesis Abstracts will be published monthly and will include abstracts from the most recently published literature.

Inquiries may be addressed as follows:

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National Cancer Institute
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NOTE

Journal names are abbreviated according to the list of abbreviations used by Index Medicus. If the journal is not covered by Index Medicus, then the abbreviations (with some modifications) found in World Medical Periodicals, 3rd Edition, are used.

ABBREVIATIONS USED IN ABSTRACTS

admin.	administered, administration	mg	milligram(s)
av.	average	min.	minute(s)
C	curie(s)	ml	milliliter(s)
mC	millicurie(s)	mm	millimeter(s)
μC	microcurie(s)	mo.	month(s)
cm	centimeter(s)	MTD	maximum tolerated dose
conc.	concentration	NIH	National Institutes of Health, USA
cpm	counts per minute	p.o.	orally
DNA	deoxyribonucleic acid	QO ₂	oxygen quotient
DNase	deoxyribonuclease	PFU	plaque forming unit
e.g.	for example	ppm	parts per million
FFU	focus forming unit	pt.(s)	patient(s)
g.i.	gastrointestinal	RBC	red blood cells (erythrocytes)
g	gram(s)	RES	reticuloendothelial system
μg	microgram(s)	resp.	respectively
Hb	hemoglobin	RNA	ribonucleic acid
i.a.	intra-arterial	RNase	ribonuclease
ID ₅₀	median infectious dose	soln.	solution
inj.	injected, injection(s)	s.c.	subcutaneous
inoc.	inoculated, inoculation(s)	TCID	tissue culture infectious dose
i.p.	intraperitoneal	x	times (e.g. x 3/wk.)
I.U.	international unit(s)	U	unit
i.v.	intravenous	UV	ultraviolet
kg	kilogram(s)	vol.	volume
LD ₅₀	median lethal dose	VA	Veterans Administration
M	molar, mole(s)	wt.	weight
mM	millimole(s)	WBC	white blood cells (leukocytes) or white blood cell count
μM	micromole(s)		
max.	maximum	yr.	year(s)

LANGUAGE ABBREVIATIONS

Af.	Afrikaans	E.	English	Hun.	Hungarian	Lith.	Lithuanian	Ser.	Serbo-Croatian
Ar.	Arabic	Eston.	Estonian	Ic.	Icelandic	Maced.	Macedonian	Sl.	Slovene
Bul.	Bulgarian	Fin.	Finnish	In.	Indonesian	Nor.	Norwegian	Sp.	Spanish
Ch.	Chinese	Fr.	French	It.	Italian	Pol.	Polish	Sw.	Swedish
Cz.	Czech	Ger.	German	Jap.	Japanese	Por.	Portuguese	Th.	Thai
Dan.	Danish	Gr.	Greek	Kor.	Korean	Rum.	Rumanian	Uk.	Ukrainian
Dut.	Dutch	Heb.	Hebrew	Latv.	Latvian	Rus.	Russian	Viet.	Vietnamese

- 70-161 EVALUATION OF THE CARCINOGENIC TOXICITY OF FOREIGN SUBSTANCES IN FOODS; A CONTRIBUTION TO METHODOLOGY. (Rum.) Galea, V. and N. Preda. Clujul Med. 41(3):347-353, 1968. (5 references)

Standards established by a joint committee of the W.H.O. and F.A.O. for the detection and toxicity testing of carcinogenic substances in foods are discussed. Methods for prevention of the carcinogenic action of foreign substances in foods are also presented. A mathematical equation to express the cumulative effects and potential carcinogenicity of such substances is included.

- 70-162 CARCINOGENIC AND CO-CARCINOGENIC PLANT PRODUCTS. I. CARCINOGENIC SUBSTANCES PRODUCED BY BACTERIA AND THALLOPHYTES (RHODOPHYCEAE AND EUMYCETES). (Ger.) Gibel, W. (German Acad. Sci. Robert Rossle Clin., Berlin) and T. Schramm. Arch. Geschwulstforsch. 32(4): 391-404, 1968. (62 references)

The occurrence, distribution, chemical structure toxicity and oncogenicity of the following substances produced by lower plants are reviewed: Ethionin, a metabolic product of many bacteria including *E. coli*; Carrageenin from Rhodophyceae (especially *Chondrus crispus*); those from Euscomycetes such as different aflatoxins from *Aspergillus flavus*, Sterigmatocystin from *Aspergillus versicolor*, Luteoskyrin from *Penicillium islandicum*, Griseofulvin from *Penicillium griseofulvum* and Streptozotocin from *Streptomyces achromogenes*. In addition, different metabolic products such as Ochratoxin, a metabolite of *Aspergillus ochrogenes*, and those produced by *Claviceps purpurea* (Euscomycetes), *Candida parapsilosis* (Ascomycetes), and *Clitocybe suaveoleus* (Basidiomycetes) (producing a naturally occurring nitrosamine compound) are discussed. It is suggested that metabolites of molds used in the production of different cheeses be investigated for possible carcinogenic activity.

- 70-163 CARCINOGENIC AND CO-CARCINOGENIC PLANT PRODUCTS. II. CARCINOGENIC SUBSTANCES SYNTHESIZED BY PTERIDOPHYTA (FILICINAE) AND SPERMATOPHYTA (CYCADINEAE, DICOTYLEDONEAE, MONOCOTYLEDONEAE). (Ger.) Schramm, T. (Inst. Cancer Res., Berlin) and W. Gibel. Arch. Geschwulstforsch. 33(2):169-188, 1969. (96 references)

The distribution, chemical structure, general pathogenic and carcinogenic and cocarcinogenic characteristics of substances produced by higher plants are reviewed and briefly discussed. These

include the strongly carcinogenic substances synthesized by *Pteridium aquilinum* (Filicinae), cycasin produced by Cycadineae (Spermatophyta), safrol produced by different species of *Sassafras*, alkaloids by *Senecio* and those of *Crotalaria* and *Heliotropium*. Lactones isolated from different species of Ranunculaceae, substances from *Trifolium subterraneum* (Papilionaceae) and from *Pueraria mirifica* (Leguminosae) with an estrogenic effect and organic sulfur compounds like thiourea (Papilionaceae) and Crucifera and tannic acid are briefly surveyed. Oil of calamus (Araceae) is carcinogenic but croton oil (Euphorbiaceae) and different citrus oils (Rutaceae) are co-carcinogenic.

- 70-164 NITROSAMINES AS ENVIRONMENTAL CARCINOGENS. (E.) Lijinsky, W. (U. Nebraska Coll. Med. Eppley Inst. Res. Cancer, Omaha) and S. S. Epstein. Nature (London) 225(5227):21-23, 1970. (23 references)

A review is presented of evidence suggesting that nitrosamines are possibly more significant in human cancer in an industrialized society than polynuclear compounds, azo dyes or aflatoxins. The authors suggest that the *in vivo* formation of nitrosamines from ingested nitrite and certain secondary amines is a potentially serious problem, and consideration should be given to reduction or elimination of one or other nitrosamine precursors, nitrites and certain secondary amines, from the diet.

- 70-165 FORMATION OF A SIGMA COMPLEX AS A HYPOTHETICAL RATE-DETERMINING STEP IN THE CARCINOGENIC ACTION OF UNSUBSTITUTED POLYCYCLIC AROMATIC HYDROCARBONS. (E.) Scribner, J. D. (U. Wisconsin Med. Ctr., Madison). Cancer Res. 29(11):2120-2126, 1969. (8 references)

The author suggests that electrophilic attack on the L-region of a polycyclic aromatic hydrocarbon is a deactivation step in its carcinogenic attack on host tissue. A review of previous work is presented to support the L-region hypothesis and to suggest that a minor role in carcinogenicity determination is played by the stability of the sigma complex.

- 70-166 The Health Consequences of Smoking. Horn, D. and A. C. Kolbye (Eds.). Suppl. Health Service Pub. No. 1696-2. U.S. Dept. Health, Education and Welfare, Washington, 1969, 98 pp., \$.50.

PHYSICAL CARCINOGENESIS

70-167 INDUCTION OF GASTRIC ADENOCARCINOMA IN MICE BY LOCALIZED X-IRRADIATION. (E.) Hirose, F. (Hiroshima U. Res. Inst. Nuclear Med. Biol., Japan). Gann 60(3):253-260, 1969.

Radiation was admin. to the gastric region of 2 groups of mice: twenty one 82-88-day-old mice received 1,500 rads at 1-week intervals x 6 (total; 9,000 rads); twenty four 59-day-old mice of both sexes received 2,000 rads x 5 at weekly intervals (10,000 rads). The total incidence of mucosal atrophy was 100% in both groups; adenocarcinoma was seen in 20% (12% in young, 28% in old); ulceration in 83% (88% and 78%); atypical hyperplasia or precancerous change in 37% (35% and 44%); squamous cell carcinoma in 3% (0% and 6%). Sixteen-week survival was seen in 17/21 older mice, 14-week survival in 18/24 younger mice. Pancreatic or mesenteric metastasis was seen in 2/7 with gastric adenocarcinoma. The incidence of gastric adenocarcinoma in the second group was 11% in males and 44% in females.

70-168 SKIN TUMOUR INCIDENCE IN CBA MICE GIVEN FRACTIONATED EXPOSURES TO LOW ENERGY BETA PARTICLES. (E.) Hulse, E. V. (Radiobiol. Res. Unit, Harwell, Berkshire, England) and R. H. Mole. Brit. J. Cancer 23(2): 452-463, 1969.

Female CBA/H mice were irradiated over the middle torso with fractionated ^{204}Tl beta particles to a total dose of 6,000 or 12,000 rads (20 equal doses; Mon-Fri x 4 consecutive weeks; weekly exposures at 7 day intervals; or monthly exposures at 4 week intervals). Tumor incidence was approximately half as great with 6,000 rads as with 12,000 rads. Earliest tumors (1 fibrosarcoma, 1 squamous carcinoma) were seen in the 9th mo. after the last of 4 monthly 3,000 rad doses; the first fibroma appeared 18 mo. after the last of 12 weekly exposures (total 12,000 rads). The peak tumor rate occurred in the second half of the second yr. or the first half of the third yr. after exposure, whether exposures were single or fractionated and whether tumors were dermal or epidermal. There was no correlation between radiation related skin damage and tumor incidence; and there was little difference between single and fractionated radiation doses in overall tumor incidence. Tumors appeared to develop more slowly after fractionated doses.

70-169 QUANTITATIVE ESTIMATION OF EXPERIMENTAL HEPATOMAS BY ^{198}Au -COLLOID. (Ger.) Matthes, T. (German Acad. Sci. Robert Rossle

Clin., Berlin), H.-J. Altenbrunn and B. Kuhn. Arch. Geschwulforsch. 32(4):353-357, 1968.

The fact that over 95% of i.v. admin. ^{198}Au -colloid is retained in the RES cells of the intact liver but only approx. 1% of radioactivity can be found in primary and secondary liver tumors was used to develop a simple method for quantitative determination of normally functioning liver tissue and of hepatomas. Hepatomas were induced in 18 male and female Wistar rats by admin. of diethylnitrosamine (5 mg/kg, total dose 500-900 mg/kg) and the percent of functioning liver tissue calculated after inj. of 15 μC ^{198}Au colloid in 0.5 ml NaCl into the tail vein. The percent of functioning varied in different animals from 10-80%. It is stressed that although exact calculations were possible in most animals, in 4/18 where tumor and nontumor tissue could not be properly divided the described method led to errors.

70-170 DEFECTIVE PHOTOCHEMICAL REPAIR IN EPITHELIUM PREDISPOSED TO FIELD CANCERIZATION. (E.) Roth, D. (Univ. Hosp., New York, N. Y.) and H. H. Sage. Cancer 24(3): 511-519, 1969.

Buccal cells obtained from 34 pts. with carcinoma of the lip, gingiva, tongue, palate, pharynx or larynx; 1 case of leukoplakia; and 3 heavy smokers with no symptoms of carcinomas exhibited varying degrees of deficient recovery as measured by dye-binding, after exposure to UV irradiation (2.5×10^4 ergs/mm² total dose). Tumor site, pt. age and sex, modality of treatment and time elapsed since therapy did not affect the dye-binding response. Buccal cells obtained from 18 nonsmoker controls recovered almost completely after UV irradiation.

70-171 ICHTHYOSIS UTERI. A CASE REPORT. (Pol.) Sikorowa, L. (Inst. Oncol., Warsaw). Nowotwory 19(1):65-70, 1969.

This is the first described case of ichthyosis uteri in the Polish literature. After diagnosis of uterine adenocarcinoma the pt. (57 yr. old.) was treated with X-rays and the uterus removed 4 weeks later. At that time the endometrial mucosa was covered with a thick layer of squamous epithelium. Since endometrial biopsy before X-ray treatment had shown several foci of "mummified" paraepidermoid squamous epithelium in addition to foci of adenocarcinoma, it is suggested that the squamous metaplasia of the endometrial epithelium was intensified by X-ray treatment, resulting in ichthyosis uteri.

70-172 THE CONDITION OF THE UPPER RESPIRATORY TRACT AMONG WORKERS OF THE TOBACCO INDUSTRY. (Pol.) Gerwel, T. (Miejskiego Hosp., Gdynia, Poland). Med. Pracy 19(6):599-606, 1968.

A study of different plants of the Poznan Tobacco Industry in Poland revealed 6-544 mg/m³ of tobacco dust in different halls and 106-198 tobacco particles/ml of air. Laryngological examination was performed on all 233 workers (85 men, 17-64 yr. old and 148 women, 17-56 yr. old) divided into 10 groups according to length of employment (from < 1 yr. to > 40 yr.). No correlation between age or length of employment and findings are presented. Only 18.6% of the workers reported minor symptoms such as frequent sore throats (17), laryngitis (7), or dryness in nose (5). No neoplastic or preneoplastic changes were found. Changes of the "smoker's throat" type were much more pronounced and more frequent among smokers than nonsmokers (erythema of different parts of the oral cavity was present in 21.07-25.37%, swelling in 12.30-14.19%). Erythema of the larynx was seen in 12.73% (29 smokers, 2 nonsmokers), thickening of the ligaments of the larynx in 16.34% (all smokers), atrophic changes of the mucous membranes of the nose and anterior part of throat in 4.3% (4 smokers, 6 nonsmokers), in the posterior part in 5.95% (7 and 6 resp.) and dryness of larynx in 1.25% (1 and 2, resp.). It is concluded that with proper preventive measures (removal of tobacco dust) no deleterious effect on the upper respiratory tract of tobacco industry workers should be expected.

70-173 RESPIRATORY TRACT RETENTION OF BLUE TETRAZOLIUM REDUCING SUBSTANCES FROM TOBACCO SMOKE. (E.) Hagopian, M. (Mason Res. Inst., Worcester, Mass.) and H. Rosenkrantz. Proc. Soc. Exp. Biol. Med. 130(4):1234-1237, 1969.

In 18 human volunteers (14 females, 18-52 yr.; 4 males, 16-33 yr.) the retention of particulate and gaseous reducing components from cigarettes smoked in their "normal fashion" was higher after pulmonary exposure than after buccal cavity exposure, as measured by blue tetrazolium. The authors discuss blue tetrazolium for use in the study of effects of tobacco on the respiratory system.

70-174 EXPERIMENTAL STUDIES OF THE TUMORIGENIC EFFECTS OF CIGARETTE-SMOKE CONDENSATES ON THE SKIN OF MICE. COMMUNICATION I: THE OVERALL STUDY. (Ger.) Döntenwill, W. (Gazellenkamp 38, Hamburg, Germany), H. Elmenhorst, H.-P. Harke, G. Reckzeh, K. H. Weber, J. Misfeld and J. Timm. Z. Krebsforsch. 73(3):265-284, 1970.

One group of 8-9 week old ICI mice was treated with cigarette-smoke condensate in acetone (0.2 ml/dose, 3 x/wk. by topical application on the back until the animals died spontaneously), representing 27.6 mg condensate/dose. A second and third group was treated in the same way, using conc. of 42.5 and 66.8 mg condensate/dose, resp. One group of control animals received no treatment and one was treated with acetone alone; other control groups were treated with benzpyrene (3 doses/wk. of 12 or 60 µg until death; 189 µg/dose, 3 x/wk. x 10 wk.; 189 µg/dose, 3 x/wk. x 25 wk.) or 7,12-dimethylbenzanthracene (140 µg, single dose). The cigarette-smoke condensate was derived fresh every week, using 12 different brands (representing typical German mixtures of tobacco), which were smoked simultaneously. Mean survival times for untreated controls and for the 3 groups of animals receiving cigarette-smoke condensate (in the order mentioned above) were 83.7, 84.1, 79.2, and 76.4 weeks, resp.; the differences for the second and third experimental groups were statistically significant. Compared to untreated controls or controls treated with acetone alone, only the incidence of skin tumors (s.c. sarcomas, papillomas and carcinomas) was increased by the weak carcinogenic activity of the cigarette-smoke condensate (total incidence of skin tumors in condensate-treated animals was 28.6%; total incidence in controls was not indicated), with a largely linear dose-response relationship for all skin tumors and for skin carcinomas alone. No significant effect was exerted on metastasis or on the incidence of tumors at other sites. Skin tumor incidence was significantly lower and both mean tumor induction and mean survival times were significantly prolonged in the condensate-treated animals, as compared to any group of controls receiving benzpyrene. When all animals treated with smoke-condensate were combined with 2 other experimental groups (one, treated with tobacco extract in ethanol + water; one, treated with 4 different fractions of tobacco extract), spontaneous regression of skin papillomas could be demonstrated in 6.6% of the overall group.

70-175 EXPERIMENTAL STUDIES OF THE TUMORIGENIC EFFECTS OF CIGARETTE-SMOKE CONDENSATES ON THE SKIN OF MICE. COMMUNICATION II: INDIVIDUAL COMPARISONS BETWEEN THE CONDENSATES OF MODIFIED CIGARETTES. (Ger.) Döntenwill, W. (Gazellenkamp 38, Hamburg, Germany), H. Elmenhorst, H.-P. Harke, G. Reckzeh, K. H. Weber, J. Misfeld and J. Timm. Z. Krebsforsch. 73(3):285-304, 1970.

Three groups of 8-9 week old ICI mice, were treated with cigarette-smoke condensate in acetone (0.2 ml/dose, 3 x/wk. by topical back application until the animals died spontaneously), representing conc. of 27.6 mg, 42.5 mg, and

66.8 mg condensate/dose, resp. Controls were either untreated or treated with acetone alone. In addition to the standard-brand cigarette employed, which had a typical German mixture of tobaccos, modifications of the test cigarette were made by changing its length, adding various filters and humectants, increasing and decreasing moisture, etc. In correlative studies, tumorigenic activity was compared on the basis of the quantities of condensate required to produce the same clinical effects. When smoked down to the same final butt length, the biological activity of the condensate was not affected by cigarette length although long cigarettes had a higher, total tumorigenic activity (with a difference approaching statistical significance), due to the fact that more tobacco was consumed. Cellulose and cellulose acetate filters had no effect on tumorigenicity; activated charcoal filters increased it slightly; all 3 types of filters decreased the total quantity of condensate, however. Tumorigenic activity was not affected by adding 2% diethylene glycol or 1% gallic acid-n-propylester to the tobacco, prior to smoking. When the moisture of unsmoked tobacco was reduced from a 12% to a 6% level, no effect was exerted; when it was increased to a 20% level, tumorigenic activity was increased significantly. Cigarettes made of reconstituted tobacco (after having mixed the tobacco with a methylene chloride and methanol combination + methylcellulose containing over 30% methoxyl, prior to drying) had a significantly less active condensate, as did the condensate of tobacco which had been extracted with ethanol and water. There was no significant relationship between tumorigenic activity and a condensate's content of either 3,4-benzpyrene or phenol. A possible relationship between tumorigenic activity and the amount of the so-called nitromethane fraction present was suggested but not fully confirmed.

70-176 EXPERIMENTAL STUDIES OF THE TUMORIGENIC EFFECTS OF CIGARETTE-SMOKE CONDENSATES ON THE SKIN OF MICE. COMMUNICATION III: ATTEMPTS TO IDENTIFY AND INCREASE THE CONCENTRATIONS OF TUMOR-INDUCING FRACTIONS. (Ger.) Döntenwill, W. (Gazellenkamp 38, Hamburg, Germany), H. Elmenhorst, H.-P. Harke, G. Reckzeh, K. H. Weber, J. Misfeld and J. Timm. Z. Krebsforsch. 73(3):305-314, 1970.

Three groups of 8-9 week old ICE mice were treated with cigarette-smoke condensate in acetone (0.2 ml/dose, 3 x/wk. by topical application until the animals died spontaneously), representing conc. of 27.6 mg, 42.5 mg and 66.8 mg condensate/dose, resp. Only the 2 higher dose levels were used for comparative purposes in the following studies. Controls were either untreated or treated with acetone alone, and comparison groups were treated with the nitromethane fraction of the condensate (Fraction V), representing 6.75 wt. percent of the whole condensate (C) and containing almost all of its

aromatic hydrocarbons (dose levels = 2.6 mg/dose and 3.9 mg/dose), a sub-fraction of V (Fraction VI), representing 1.08 wt. percent of C and containing > 85% of its aromatic hydrocarbons (dose levels = 0.3 mg/dose and 0.44 mg/dose), the recombination of C after fractionation (R; dose levels = 41.4 mg/dose and 64.2 mg/dose), R without V (R-V; dose levels = 38.6 mg/dose and 59.9 mg/dose) and R without VI (R-VI; dose levels = 41.1 mg/dose and 64.4 mg/dose). In terms of tumorigenic effectiveness, as compared to C, R had lost 0.8%-1.0% of its activity. V was 17 times as active as C and 42.5 times as active as R-V, while C was 2.5 times as active as R-V. VI was 50 times as active as C and 90 times as active as R-VI, while C was approx. twice as active as R-VI. VI was 3 times as active as V. Note is made that V was by no means composed solely of aromatic hydrocarbons, but contained a large number of substances of varying polarities, including the nicotine alkaloids and other water soluble compounds. The nicotine content was 4.3%; the phenol content, 0.47%. Although Fraction V accounted for almost all the tumorigenic activity of C, only approx. 50% of that activity was carried over into Fraction VI, so that R-VI was significantly more active than R-V, appearing to confirm that substances other than the aromatic hydrocarbons are also responsible for the induction of skin tumors in mice.

70-177 THE MOUSE SKIN CARCINOGENICITY OF CIGARETTE SMOKE CONDENSATE: FRACTIONATED BY SOLVENT PARTITION METHODS. (E.) Whitehead, J. K. (Tobacco Res. Council Labs., Harrogate, Yorkshire, England) and K. Rothwell. Brit. J. Cancer 23(4):840-857, 1969.

A description is presented of three methods of fractionation for the concentration of polycyclic aromatic hydrocarbons of cigarette smoke condensate. Two methods resulted in the separation of cyclohexane soluble material (fraction G), which was 24% of the original smoke condensate, from water soluble and methanol soluble constituents. Fraction G contained a high percentage of the tumorigenic components found in cigarette smoke, as indicated by mouse skin painting tests. The authors consider Fraction G the most satisfactory material for further attempts to isolate the mouse skin carcinogenic factors in cigarette smoke. No effect on the incidence of spontaneously occurring tumors was seen in any of the treated mice.

70-178 HISTOLOGIC CHANGES IN THE LARYNX IN RELATION TO SMOKING HABITS. (E.) Auerbach, O. (VA Hosp., East Orange, N. J.), E. C. Hammond and L. Garfinkel. Cancer 25(1): 92-104, 1970.

In 942 men who came to autopsy between 1964 and 1967, microscopic changes in the larynx were

seen most often in cigarette smokers. The changes increased in proportion to the number of cigarettes smoked/day before death, and were more prevalent in cigarette smokers than in pipe or cigar smokers. Ex-smokers had fewer changes than those men who smoked up to the time of death. Atypical changes in the epithelial cells of the larynx were seen mostly in the true vocal cord and, to a lesser extent, in the false vocal cord, and the area of the larynx above the vocal cord. The least changes were seen in the area below the vocal cord. Histologic changes included atypical nuclei, carcinoma in situ and early invasive carcinoma. Cells with disintegrating nuclei were found mainly in ex-cigarette smokers.

70-179 LUNG CANCER: SMOKING AND OTHER ASSOCIATED FACTORS. (E.) Hems, G. (Univ. Med. Bldgs., Aberdeen, Scotland). Brit. J. Cancer 23(4):661-669, 1969.

Inspection of previously collected data from 20 countries indicated that consumption of cigarettes, other tobacco, and solid fuel explained almost half the variation in lung cancer mortality; the variation explained was increased to 80% when stomach cancer mortality was included. A model was developed and it was predicted that cigarettes accounted for 70% as a causative factor in lung cancer; other tobacco products, 10%; and consumption of solid fuel, 20%. Lung cancer in males aged 20-24 yr. was associated with solid fuel consumption and rates of mortality from stomach cancer and bronchitis.

70-180 EFFECT OF BENZOPYRENE, CIGARETTE SMOKE CONDENSATE AND PASSIVE (FORCED) SMOKING ON PRODUCTION OF ZOXAZOLAMINE HYDROXYLASE. (Ger.) Döntenwill, W. (Cigarette Indust. Inst. Sci. Res., Hamburg, Germany), H.-P. Harke, U. Lafrenz and G. Reckzeh. Experientia 25(7): 714-715, 1969.

Baseline zoxazolamine hydroxylase (ZH) activity (measured by the duration of zoxazolamine paralysis) was higher in the livers of male Syrian hamsters than in the livers of male Wistar AF/Han rats, but hepatic ZH was more inducible in the rats than in the hamsters. Shortening of zoxazolamine paralysis by pretreatment with 3,4-benzpyrene (BP; 10 mg/kg i.p.), inj. of cigarette smoke condensate (40 mg/kg i.p.) or 12 sessions of passive forced cigarette smoking (30 cigarettes/session in rats, 3 each in hamsters), was greater in the rats than in the pretreated hamsters. ZH activity was decreased following partial hepatectomy and stimulated by cigarette smoking, admin. of BP and inj. of the cigarette smoke condensate. The level of ZH activity was not related to the amount of hydrocarbon present in the smoke. Since ZH activity varied widely between animals, it is concluded that the detoxification of aromatic hydrocarbons depends

not only on their solubilities and their persistence in the liver, but also on the detoxifying capacities of the individual livers.

70-181 FINDING AND CHARACTERIZATION OF ASBESTOS PARTICLES IN PLEURAL MESOTHELIOMAS. (Fr.) Le Bouffant, L. (Ctr. Res. Coal Mines France, Oise), H. Daniel-Moussard, S. Durif, J.-C. Martin, C. Normand and A. Policard. C. R. Acad. Sci. D (Paris) 268(18): 2269-2274, 1969.

Successful electron microscopic detection of asbestos particles in conventional histologic samples of pleural mesothelioma is highly unlikely, due to the thickness of the sample and the chances of sectioning the particles in the course of preparing it. A method for detecting such particles involves incinerating a sample in air in a platinum crucible (450 degrees C x 15 hours, then 600 degrees C x 3 hours), subjecting the residue to treatment with 12 N HCl, prior to evaporating, washing with distilled water, and filtering on a cellulose membrane with micropores covered by a carbon deposit. The sample can then be prepared for microscopic examination and analysis by electronic microdiffraction, after dissolving the cellulose in an organic solvent. Some forms of asbestos, such as chrysotile, are partially attacked by HCl. Detection of these requires X-ray diffraction analysis of a supplementary sample of approximately 10 µg, removed from the product of incineration (above) or from the residue left after treatment with the acid. This supplementary sample can also be derived by incineration at 150 degrees C in a plasma kiln, under a pressure of 3-5 torr of oxygen. When this latter method is used, the hydrated minerals do not undergo significant changes.

70-182 CORRELATION BETWEEN LUNG ASBESTOS COUNT AT NECROPSY AND RADIOLOGICAL APPEARANCES. (E.) Macpherson, P. (Western Infirmary, Glasgow) and J. K. Davidson. Brit. Med. J. 1(5640):355-357, 1969.

Of 100 pts. who had chest X-rays within 1 yr. of death, 44 had positive asbestos counts at necropsy. Evidence of asbestosis was seen on radiographs in 8/9 who had asbestos counts of > 40 at necropsy.

70-183 MESOTHELIOMAS IN RATS FOLLOWING INOCULATION WITH ASBESTOS. (E.) Wagner, J. C. (Llandough Hosp., Penarth, Glamorgan, Wales) and G. Berry. Brit. J. Cancer 23(3):567-581, 1969.

Six-week-old SPF Wistar rats and standard rats were inj. intrapleurally with 20 mg amosite (A) asbestos dust, chrysotile (C) dust, crocidolite (CR) dust, extracted crocidolite (CR) or saline,

and each animal was allowed to live until natural death or appearance of distress. Mesotheliomas developed in over half the animals inj. with C and the CRs; but less than half the A inj. animals developed mesotheliomas. No mesotheliomas were seen in saline inj. controls. Inj. site sarcomas, contributed to faulty inj. technique developed in a small percentage of asbestos treated animals. Survival patterns were similar for each dust except for variations in time to initial mesothelioma (initial time was longer with A then with C and CRs). After the initial mesothelioma a rapid onset of cases occurred, resulting in 50% mortality in the next 300 days. No differences were seen between males and females and SPF and standard rats nor between the natural and oil extracted CR.

70-184 SUBSTRATE AND PHENOBARBITAL INDUCIBLE AFLATOXIN-4-HYDROXYLATION AND AFLATOXIN METABOLISM BY RAT LIVER MICROSOMES. (E.) Schabert, J. C. (Nat. Nutrition Res. Inst., Pretoria, South Africa) and M. Steyn. Biochem. Pharmacol. 18(9):2241-2252, 1969.

In male albino Wistar rats admin. aflatoxin B₁ (AB; 500 µg/kg/day x 5, i.p.) and sacrificed on day 5, the hydroxylation of AB in the liver was 3.5 times higher than in controls. Hydroxylase activity was located in the microsomal fraction of the liver. After 20 hr. incubation < 20% of the original amount of AB was left in the incubation mixture. In rats admin. phenobarbital (P, 75 mg/kg/day x 5, i.p.) hydroxylation was increased 2.3 times. P was not significantly metabolized by rat liver microsomes. Induction of aflatoxin 4-hydroxylase activity after P and AB was restricted to the microsomal fraction. The authors suggest that aflatoxin M₁, M₂ and "Gm", could be intermediates in the breakdown of AB.

70-185 AFLATOXIN CARCINOGENESIS: INHIBITION OF LIVER CANCER INDUCTION IN HYPOPHYSECTOMIZED RATS. (E.) Goodall, C. M. (U. Otago Nat. Cancer Res. Labs., New Zealand) and W. H. Butler. Int. J. Cancer 4(4):422-429, 1969.

Random-bred male MRC albino rats were weaned at 4 wk. of age, at which time they were either left intact or hypophysectomized. At 8 weeks of age, all rats began to receive aflatoxin at 4 µg/g diet. Assay of extractable aflatoxins showed 45% aflatoxin B₁, 45% G₁, 5% B₂ and 3% G₂. Hepatic carcinoma developed in 14/20 intact rats and in 0/37 hypophysectomized rats, although both groups developed extrahepatic tumors (1 each of renal carcinoma, adrenal adenoma and lymphoma in intact rats; 4 lacrimal gland carcinomas and 1 tracheal carcinoma in hypophysectomized rats). Hypophysectomized rats survived longer than intact animals and therefore received a larger cumulative dosage of aflatoxin. Livers of intact rats showed toxic

lesions similar to those described previously and by 35-40 weeks these lesions often could not be distinguished from early tumors. The first microscopic carcinoma was seen after 37 weeks, while a benign biliary cystadenoma was seen at 41 weeks. Fully developed metastasizing hepatocellular carcinoma was first seen at 49 weeks in a rat dying from secondary peritoneal hemorrhage. Metastasis to lungs and mesenteric lymph nodes was seen in 9/14 with definite carcinoma.

70-186 EFFECT OF AFLATOXIN B₁ ON THE INCORPORATION OF ¹⁴C-ACETATE INTO CHOLESTEROL BY RAT LIVER. (E.) Kato, R. (Nat. Inst. Hyg. Sci., Tokyo), K. Onoda and Y. Omori. Experientia 25(10):1026, 1969.

In male Wistar rats admin. aflatoxin B₁ (A; 3 or 5 mg/kg; i.p.) in dimethylsulfoxide and sacrificed 24 hours after inj. the incorporation of 1-¹⁴C-acetate into cholesterol of liver slices was reduced to 10% of control values. Similar results were seen with 2 mg/kg A; but 0.5 mg/kg did not produce a significant decrease. Content of liver cholesterol was slightly increased by A, but serum cholesterol was decreased.

70-187 AFLATOXIN INDUCED LESIONS IN SYRIAN HAMSTERS. (E.) Herrold, K. M. (NCI, Bethesda, Md.). Brit. J. Cancer 23(3): 655-660, 1969.

One-mo.-old male and female Syrian hamsters were admin. aflatoxin (A; 0.1 mg in 50% ethanol biweekly x 10-11 mo., Intragastrically; or 0.2 mg in 50% N,N-dimethylformamide weekly x 6-8.5 mo., i.p.). Control groups received only the solvents. Lesions of the liver, kidney, small intestine, Harderian gland and the periodontal membrane developed in A-treated animals. Av. life span was 20 mo. for intragastrically treated animals and 11 mo. for i.p. treated animals. Focal hemorrhagic necrosis, hemosiderin deposits, megalocytosis and bile duct proliferation occurred in the liver. Cytomegalic changes in the proximal tubules were seen in the kidney lesions, and epithelial nests of Malassez were seen in the periodontal membrane. Solid and papillary cystadenomas were seen in the Harderian gland.

70-188 AFLATOXIN B₁ CARCINOGENESIS IN LIPOTROPE-DEFICIENT RATS. (E.) Rogers, A. E. (Massachusetts Inst. Tech., Cambridge, Mass.) and P. M. Newberne. Cancer Res. 29(11):1965-1972, 1969.

Beginning at 6 weeks of age male Fischer rats were fed either a lipotrope-deficient diet or a control diet inducing borderline lipotrope deficiency. Aflatoxin B₁ (A; 25 µg/day for 5 days/week x 3 weeks or 1/week x 15 weeks; total

dose 375 µg) was admin. by gastric intubation to both groups at 18 weeks of age. Rats were sacrificed from 24 hours to 1 yr. after the last A dose. Deaths in animals on the control diet appeared to be from hepatocarcinomas in all cases; deficient rats had no hepatocarcinomas at death. Malignant hepatic tumors were first found in sacrificed rats from both diets at 6 mo., and by 12 mo. incidence was 100% in both groups. An early hyperplastic hepatocytic response was seen in control diet animals, and it persisted to time of carcinoma development; it was not found in deficient animals.

70-189 THE EFFECT OF AFLATOXIN ON FERMENTATION IN THE RUMEN. (Fr.) Fehr, P.-M. (Nat. Inst. Agronom., Paris) and J. Delage. C. R. Acad. Sci. [D] (Paris) 270:550-553, 1970.

When raw extract of peanut oil cake containing aflatoxin B₁ (0.37 or 0.60 µg/ml of incubation mixture) was incubated with 1 g hay + 20 ml juice from the rumen (source not specified) + 20 ml artificial saliva, at 39 degrees C x 24 hours under nitrogen, cellulolysis was diminished significantly, as compared to controls in which the extract was either lacking or uncontaminated with aflatoxin. Also significantly reduced were the total production of volatile fatty acids (VFA) and the percentage of acetic acid in that total, although the percentage of propionic acid was significantly increased. As compared to the extract-free control, an equal vol. of the uncontaminated extract had no significant effect on any of these values, while both the contaminated and the uncontaminated extracts decreased the butyric and increased the valeric acid percentages of total VFA. The effects of aflatoxin were demonstrably dose related. In a correlative experiment, increasing the conc. of aflatoxin B₁ above a threshold level of 0.05 µg/ml incubation fluid progressively and significantly diminished both cellulolysis and the production of ammonia in the course of fermentation.

70-190 TIME COURSE OF ALTERATIONS OF RAT LIVER POLYSOME PROFILES INDUCED BY AFLATOXIN B₁. (E.) Pong, R. S. (Massachusetts Inst. Tech., Cambridge, Mass.) and G. N. Wogan. Biochem. Pharmacol. 18(10):2357-2361, 1969.

Aflatoxin B₁ (3 mg/kg (LD₅₀) i.p. in a single dose) in 0.05 ml dimethylsulfoxide admin. to male Fischer rats (sacrificed by decapitation 0.5 hr. - 5 days after inj.) caused marked disaggregation of liver polysomes at 3 hr. which persisted until 36 hr. after admin. Monomer and dimer areas of the polysome profile returned to control levels after 72 hr. but polysome reaggregation was not complete until 5 days after inj.

70-191 HEPATIC CARCINOGENESIS THRESHOLD AND BIPHASIC MITOCHONDRIAL SWELLING RESPONSE IN THE GUINEA-PIG DURING DIETHYL-NITROSAMINE ADMINISTRATION. (E.) Arcos, J. C. (Tulane U. Sch. Med., New Orleans, La.), M. F. Argus, and J. B. Mathison. Experientia 25(3): 296-298, 1969.

Random-bred male smooth-haired guinea pigs received diethylnitrosamine (DEN) in their drinking water (0.042 ml/l) with a mean daily intake of 1.2 mg. Animals received DEN supplemented with ascorbic acid for 4-24 weeks, and were sacrificed 12 mo. after first dose. No hepatic tumors were seen in animals receiving DEN for less than 8 weeks (total dose less than 58 mg), while the incidence was 21% in those receiving DEN for more than 12 weeks (113 mg). The minimal effective tumor dose was 86 mg (onset of tumorigenesis at 8-10 weeks) and the 50% tumor dose was 122 mg. The hepatic mitotic index was found to increase with increasing cumulative DEN dose, peaking at 13 weeks; no observations were made beyond 20 weeks. Two types of mitochondrial swelling were observed in hepatic cells: the first peaked at 2-3 weeks, decreased, peaked again, and terminated at 8-10 weeks; the second showed a sharp rise to a peak at 11-13 weeks. Both types of swelling were apparently required for the onset of neoplasia, which was observed to begin during the transition period between the two phases.

70-192 SEQUENTIAL EFFECTS OF CHEMICALLY DIFFERENT CARCINOGENS, DIMETHYL-NITROSAMINE AND 4-DIMETHYLAMINOAZOBENZENE, ON HEPATOCARCINOGENESIS IN RATS. (E.) Takayama, S. (Cancer Inst., Tokyo) and T. Imaizumi. Int. J. Cancer 4(4):373-383, 1969.

To study the sequential effects of 2 chemically different carcinogens on liver tumor induction, single and combined dosage regimens were used in 8-week-old Donryu rats fed N-nitrosodimethylamine (DMN; 100 µg/g diet) and/or 4-dimethylaminoazobenzene (DAB; 600 µg/g diet). A schedule of DAB for 0.62-2.5 mo., followed by DMN for 5 mo., produced far more hepatic tumors, after a shorter latency, than either DAB alone for 2.5 mo. or DMN alone for 5-10 mo. A similar situation obtained when 0.62-1.25 mo. of DMN was followed with 5 mo. of DAB, compared with either alone, as above. In rats fed DMN alone for 10 mo., 66.7% of tumors were nonepithelial, while in rats fed DAB alone for 5 mo., 100% of tumors were typical hepatomas. In rats given DAB for 2.5, 1.25 and 0.62 mo., resp., followed by DMN for 5 mo., 71-87% of induced liver tumors were epithelial, suggesting that the initial admin. of DAB may determine the type of tumor irrespective of the subsequent 5-mo. admin. of DMN. No effect on tumor type was seen with initial admin. of DMN for 1.25 or 0.62 mo., but 50% of induced tumors were nonepithelial when DMN was admin. for 2.5 mo., preceding 5 mo. of DAB. Apparently

a prolonged primary exposure to DMN can shift the pattern of induced tumors.

- 70-193 ELECTROPHORETIC CHARACTERIZATION OF ALKALINE PROTEINS IN ACIDIC CYTOPLASMIC EXTRACTS OF RAT HEPATOMA AND NORMAL RAT LIVER. (Ger.) Schwenke, K.-D. (Nutr. Inst., Potsdam-Rehbrücke, Germany). Z. Naturforsch. [B] 24(4):432-435, 1969.

Improved separation of proteins from normal rat liver and 2 transplantable rat liver carcinomas (DAENA 7330 and Berlin Hepatoma) was achieved by electrophoresis of acid extracted cytoplasmic fraction using unbuffered soln. of KCl/KOH. The isoelectric point of the carcinogen binding, growth inhibiting alkaline liver protein fraction (h-protein) was 8.3-8.4 as determined by free electrophoresis in a 0.05 M KCl/KOH system. This fraction was either absent or present in very small amounts in extracts from the 2 tumors. Using starch gel electrophoresis in 0.01 N HCl, the acid soluble cytoplasmic proteins from normal liver and the 2 hepatomas were separated into 5-6 sharply differentiated zones.

- 70-194 THE EFFECT OF HEPATOTROPIC CARCINOGENS ON A RIBOSOMAL FERRITIN FRACTION. (Ger.) Domschke, W. (U. Marburg Med. Clin., Germany) and J. G. Meyer-Bertenrath. Naturwissenschaften 56(11):564-565, 1969.

Disc electrophoresis on polyacrylamide gel usually results in separation of the ribosomal iron protein fraction into one main and 2 minor bands. The electrophoretic anodic mobility of the main band and of one secondary band decreased while one band disappeared completely after admin. of N-nitrosomorpholine (NNM) or diethylnitrosamine (DNA) for 6 weeks and thioacetamide (TAA) for 60 days (in doses which usually cause primary carcinomas) to Sprague-Dawley rats (no further details). The fraction from precancerous liver, when subjected to a protein extraction procedure dissociates into 4 disc electrophoretic bands while that from normal liver gives 6 bands indicating an alteration in protein chemistry. All products of protein extraction showed increased electrophoretic mobility when compared to the native ferritin fraction. In addition, the nucleoprotein bands from precancerous liver also differed from normal. Measurement of ribonuclease activity gave an elevated Michaelis constant probably caused by stronger masking of surface RNA structures by the altered protein components. It is concluded that the alteration of the ribosomal ferritin fraction during carcinogenesis is qualitatively identical whether induced by NNM, DNA or TAA, although the mechanism of action of these carcinogens probably differs. It is also suggested that a causal relationship exists between the observed alterations and neoplastic changes.

- 70-195 HISTOCHEMICAL INVESTIGATIONS OF CARCINOGENESIS IN RAT LIVER AFTER CONTINUOUS APPLICATION OF DIETHYLNITROSAMINE. (Ger.) Friedrich-Freksa, H. (Max Planck Inst. Virus. Res., Tübingen, Germany), W. Gössner and P. Börner. Z. Krebsforsch. 72(3):226-239, 1969.

Diethylnitrosamine was admin. by stomach tube to 78 female 3-5 mo. old Sprague-Dawley rats in either 2.8 mg/kg, 5 mg/kg, 8 mg/kg or 14 mg/kg daily doses. Clearly delineated islands of cells lacking glucose-6-phosphatase activity were observed after a total 200, 210, 240 and 255 mg dose resp. (after 84, 49, 35 or 21 days, resp.). Almost all tumors (hepatocellular carcinomas and solid undifferentiated carcinomas) which appeared after a total dose of 402, 580, 770 or 1140 mg resp. (168, 140, 112 and 98 days, resp.) also lacked glucose-6-phosphatase activity. Periodic histochemical examinations revealed a steady increase in size and number of cells lacking this enzyme until approx. 40% of parenchyma was affected. These islands were most frequently located in a 60 degree sector around the central vein. Glycogen, which no longer responded to fasting accumulated in these enlarged vacuolated cells but disappeared a few weeks later. The cytoplasm became basophilic, mitosis accelerated and cell atypia became pronounced (microcarcinomas) and a short time later typical carcinomas evolved. No regressive degeneration of liver parenchyma was seen.

- 70-196 SPECIFIC GRAVITY OF LIVER CELLS DURING HEPATOCARCINOGENESIS BY N-NITROSDIETHYLAMINE IN RATS. (E.) Imaizumi, T. (Cancer Inst., Tokyo) and S. Takayama. Gann 60(5):499-502, 1969.

Fifteen 8-week-old male Donryu rats were fed N-nitrosodiethylamine (DEN) dissolved in drinking water for 2 or 5 mo. resp. (total was 13 and 36 mg/rat, resp.). The specific gravity of liver cells was determined 4 and 8 mo. after consuming the 13 mg dose and 1 and 3 mo. after consuming the 36 mg dose. Control livers were studied after 6, 8, and 10 mo. Normal rat liver cells had a constant specific gravity of 1.085 as determined by the multistrata centrifugation method while livers from the DEN-fed animals showed a lower, widely ranging specific gravity (1.060-1.085). The results indicate that when hyperplastic changes are more pronounced the range of distribution of specific gravity of hepatic cells become wider and is always characterized by a decrease.

- 70-197 EFFECT OF HEPATOCARCINOGENS ON HEPATOCYTE DNA SYNTHESIS AND CORTISONE INDUCTION OF TRYPTOPHAN OXYGENASE. (E.) Kizer, D. E. (Samuel Roberts Noble Found., Inc., Ardmore, Okla.), B. Cox, B. A. Howell and B. C. Shirley. Cancer Res. 29(11):2039-2046, 1969.

Thioacetamide and the azo dyes 3'-methyl (3'-Me) and 4'-fluoro (4'-F) derivatives of 4-dimethyl-aminoazobenzene (DAB) when fed for 12 weeks to 140-180 g Holtzman rats (conc. in diet 0.07% and 0.06% resp.) increased hepatocyte DNA synthesis (autoradiographic demonstration of tritium 3'-thymidine incorporation), inhibited cortisone induction of tryptophan oxygenase and stimulated hepatic adenosine monophosphate (AMP) deaminase activity indicating proliferation among hepatic parenchymal cells. 4'-Me-DAB and 4'-F-DAB (added to riboflavin poor diets) showed none of these effects. Marked stimulation of DNA synthesis, inhibition of cortisone induced tryptophan oxygenase and stimulation of AMP oxygenase activity was also obtained after i.p. inj. of thioacetamide or 3'-Me-DAB (50 mg/kg/day and 250 mg/kg, resp.) but not after inj. of 4'-MeDAB or 4'-F-DAB. Simultaneous inj. of ethionine (250 mg/kg) with thioacetamide (50 mg/kg) inhibited DNA synthesis. During liver regeneration in partially hepatectomized animals only insignificant increases in AMP deaminase activity. It is concluded that hepatocarcinogens stimulate hepatocyte DNA synthesis and increase hepatic AMP deaminase activity and that the metabolism associated with DNA synthesis initiated by hepatocarcinogens differs (at least quantitatively) from that initiated by partial hepatectomy.

70-198 INTERFERENCE OF *Cysticercus fasciolaris* IN THE FORMATION OF HEPATIC LESIONS IN RATS, INDUCED BY P-DIMETHYLAMINOAZOBENZENE (DAB). (E.) Altman, R. F. A. (Oswaldo Cruz Inst., Rio de Janeiro, Brazil) and I. Ballini-Kerr. Arch. Geschwulstforsch. 33(2):113-118, 1969.

Three groups of 10 Wistar rats (100 days old) were used to test the effect of phospholipids and cholesterol on induction of hepatomas by DAB. Group I served as control, group II was pretreated for 1 mo. with Asolectin (a phosphatide) soln. as drinking water and group III was pretreated with cholesterol (4 g/kg ration). DAB was then fed to all in approx. 20 mg/day dose. Animals were killed after 3-25 weeks of DAB feeding and livers examined histologically. It was unexpectedly found that the livers of groups I and II were infested with *Cysticercus fasciolaris*. Malignant hepatic lesions were observed in infected animals after only 12 weeks of DAB feeding while livers of parasite-free rats (group III) showed only slight lesions which, even after 25 weeks of DAB, did not undergo malignant changes. It is suggested that the parasite accelerates the hepatoma inducing activity of DAB either by its metabolic products or destructive action on hepatic tissue.

70-199 ON THE UNIMPAIRABLE RESISTANCE OF THE GUINEA PIG TO DIETARY AMINO AZO DYE HEPATOCARCINOGENESIS. (E.) Gosch, H. H. (U. Michigan Med. Sch., Ann Arbor), J. C. Arcos and M. F. Argus. Z. Krebsforsch. 73(3):215-217, 1970.

The livers of 20 partially hepatectomized and 8 sham operated guinea pigs fed a diet containing 0.12% 3'-methyl-4-dimethyl-aminoazobenzene for 1 mo. before operation and 7 mo. after were perfectly normal without any trace of cirrhosis, fatty infiltration or nodules.

70-200 INCORPORATION OF TRITIATED DIMETHYL-NITROSAMINE INTO SUBCELLULAR FRACTIONS OF MOUSE LIVER AFTER LONG TERM ADMINISTRATION OF DIMETHYLNITROSAMINE. (E.) Takayama, S. (Cancer Inst., Tokyo) and M. Muramatsu. Z. Krebsforsch. 73(2):172-179, 1969.

Male ICR mice were admin. dimethylnitrosamine (DMN; 50 ppm) in peanut oil in the diet from 8 weeks of age to sacrifice (1, 3 and 7 days, and 2-37 weeks from start of the experiment). The diet was withdrawn 12 hr. before sacrifice and ^3H -DMN (100 μC ; i.p.) was admin. 1 hour before. Initially (day 3), vacuolation of the cytoplasm in the centrilobular zone and amorphous liver cells with swollen nuclei were seen. By 2 weeks the general liver pattern was similar to controls. Obvious liver cell damage in the centrilobular area became apparent by the third week. Swelling of sinusoidal endothelial cells was seen by week 10, and small blood filled cysts appeared at week 15. After 20 weeks enlarged liver cells were seen. A hemangio-endothelial sarcoma was found in 1 animal sacrificed at 37 weeks. The highest specific activity was found in the supernatant fraction 1 hr. after ^3H -DMN injection. The mitochondrial fraction had slightly less activity followed by the microsomal and nuclear fractions. Little radioactivity could be extracted from the nuclear fraction by washing, suggesting that the radioactivity was firmly bound to the nucleic acids or proteins. However, 50-80% of the radioactivity was recovered by washing from the other three fractions.

70-201 RIBONUCLEIC ACID AS AFFECTED BY HEPATOCARCINOGENESIS. (E.) Dessev, G. N. (Acad. Sci. Biochem. Res. Lab., Sofia) B. M. Mullock, E. Reid and M. K. Turner. Brit. J. Cancer 23(3):597-615, 1969.

RNA activity was studied in hepatomas and in livers of young adult albino male rats fed DL-ethionine (0.25%), α -naphthylisothiocyanate (0.075%) or azo-dyes (0.075%). The rate of RNA synthesis fell with acute treatment. A marked rise in RNA synthesis was seen in hepatomas. Actinomycin D depressed the rate of synthesis in ethionine-fed rats. The ratio of nuclear RNA to DNA was depressed in ethionine induced hepatomas and in ethionine fed rats. A decrease in microsomal RNA was seen with azo-dyes. After labeled orotate injection, postmicrosomal RNA was more highly labeled than microsomal RNA in hepatomas and liver.

70-202 SERUM ZINC LEVELS IN HEPATOCELLULAR CARCINOMA. (E.) Dunn, J. A. (U. Witwatersrand, Johannesburg, South Africa), M. C. Kew, J. D. Taylor and R. C. Mallet. Brit. J. Cancer 23(3):634-637, 1969.

Serum zinc levels were determined in 31 male Bantu pts. with primary hepatocellular carcinoma and in normal controls. No significant differences in levels were found. However, 4/31 pts. had markedly increased (205-350 $\mu\text{g}\%$) serum zinc levels. No correlation between serum zinc levels and any therapy was found.

70-203 ISOLATION OF MEMBRANE-ASSOCIATED TUMOUR-SPECIFIC ANTIGEN FROM AN AMINOAZO-DYE-INDUCED RAT HEPATOMA. (E.) Baldwin, R. W. (U. Nottingham, England) and M. Moore. Int. J. Cancer 4(6):753-760, 1969.

Homogenization by nitrogen cavitation of cells of a transplanted rat hepatoma (D23) originally induced by 4-dimethylaminoazobenzene, released membrane fractions retaining hepatoma-D23-specific antigen (13-17% of that expressed on intact tumor cells). Antigen was equally distributed between small particle and large particle fractions. Soluble cytoplasmic fractions had no detectable antigenic activity.

70-204 INHIBITION OF THE PROLIFERATIVE ACTIVITY OF PARTIALLY RESECTED LIVER BY MEANS OF DIETHYLNITROSAMINE. (Ger.) Rabes, H. (U. Munich Path. Inst., Germany), R. Hartenstein and P. Scholze. Z. Krebsforsch. 73(3):239-241, 1970.

Male Wistar rats, weighing 100-120 g at the start of the experiment, received diethylnitrosamine in their drinking water (5 mg/kg/d x 20) prior to the performance of a two-thirds hepatectomy. Beginning 20 hours after the operation, they were inj. i.p. with tritiated 6-thymidine (100 $\mu\text{C}/\text{dose}$) every 6 hours through the 56th hour post hepatectomy. Final determinations of glucose-6-phosphatase activity and DNA synthesis were made 60 hours post hepatectomy. In contrast to partially hepatectomized controls, in which DNA synthesis was demonstrable throughout the entire lobe, DNA synthesis in the treated animals was confined to those peripheral cells of the liver lobule which showed the strongest glucose-6-phosphatase activity. Intermediate and centrally located cells appeared to have lost their ability to proliferate. Further studies will be needed to determine whether this phenomenon was due to a diethylnitrosamine-mediated loss of the cells, physiologic regulatory capacities, thus constituting the first indication of the operation of a malignant process, or if it was merely a result of a generalized reaction to nonspecific traumatization.

70-205 THE EFFECT OF EXTRACTS OF AIRBORNE DUST AND SEVERAL POLYAROMATIC HYDROCARBONS ON THE BREAKDOWN OF BENZO(a)PYRENE BY RAT LIVER MICROSOMAL ENZYMES IN VITRO. (Ger.) Tomingas, R. (U. Dusseldorf Med. Inst., Germany) and W. Dehnen. Z. Krebsforsch. 73(3):242-247, 1970.

Female Wistar rats, aged 30-60 days at the start of the experiment, received a single i.p. inj. of benzo(a)pyrene (BP = 100 μg in 1 ml tricaprilyn) 24 hours before sacrifice. The metabolism of BP by liver microsomes from these rats was inhibited 16.8% when 0.3 ml ethanol was included in the incubation mixture (3.8 ml). Smaller amounts of ethanol exerted no effect; larger ones increased inhibition progressively, up to 98.9% with 1.5 ml ethanol. The addition of 625 μg extract of airborne dust to an incubation soln. containing 0.1 ml ethanol, as above, inhibited BP metabolism by 34%. No effect was exerted by the addition of 250 μg extract or 100 μg of 1 of 5 fractions. However, the addition of 100 μg of the other 4 fractions, individually, inhibited BP metabolism by 12-50%. The fraction exerting the greatest degree of inhibition contained anthracene, phenanthrene, pyrene, benzo(a)anthracene, benzo(e)pyrene, BP and dibenzo(a,h)anthracene, although the addition of 25 μg synthetic pyrene + 12.5 μg of each of the other 6 hydrocarbons had no effect on an identical incubation soln. When tested individually, none of these synthetic hydrocarbons exerted any inhibitory effect at dose levels of 20-60 μg . Anthracene and benzo(e)pyrene exerted no inhibitory effect at dose levels up to 125 μg ; dibenz(a,h)anthracene exerted no effect at 60 μg , the highest level tested. At 62.5 and 125.0 μg , the inhibitory effects of benzo(a)-anthracene were 71.8% and 80.3%, resp.; those of phenanthrene were 33.0% and 33.9%, resp. Pyrene inhibited BP metabolism by 26.2% at a dose level of 125 μg . The inhibitory effects of 3-methylcholanthrene ranged from 24.8% at 20 μg to 90.6% at 83 μg , the highest level tested.

70-206 IN CONTRAST TO RESERPINE, YOHIMBINE DOES NOT MODIFY CHEMICALLY INDUCED CARCINOGENESIS OF THE LIVER IN THE RAT. (Fr.) Lacassagne, A. (Pasteur Inst., Paris) N. P. Buu-Hoï, and N. Ba Giao. C. R. Acad. Sci. [D] (Paris) 270(5):746-747, 1970.

Nine male Wistar rats, weighing 270-310 g at the start of the study, were fed a protein- and riboflavin-impooverished diet containing p-dimethylaminoazobenzene (DAB = 0.6 g/kg) + yohimbine (an alkaloid resembling reserpine in structure 16 mg/kg). When the animals were sacrificed after 15-127 days, there was no evidence as compared to control animals, of significant effect of yohimbine on the speed with which various stages of experimental liver

carcinogenesis developed, or on the occurrence of such carcinogenesis. A similar nonsignificant effect was demonstrated when 6 male Wistar rats, weighing 280-290 g at the start of the study, were fed yohimbine (16 mg/kg diet) and at the same time receiving diethylnitrosamine (DEN = 50 mg/l) added to their drinking water. This second group of animals was sacrificed after 56-191 days, with 1 animal dying spontaneously on d 190. Inasmuch as reserpine is known to accelerate DAB-induced liver carcinogenesis, while retarding hepatic carcinogenesis induced by DEN, the lack of response to yohimbine suggests that these effects of reserpine may be indirect, involving the effects of the alkaloid on the central nervous system and certain endocrine functions (especially that of the adrenal cortex).

- 70-207 EXPERIMENTAL STUDIES ON THE EFFECT OF INITIAL DOSES OF DMBA ON THE RESPIRATORY TRACT OF SYRIAN GOLDEN HAMSTERS. (Ger.) Döntenwill, W. (Gazellenkamp 38, Hamburg, Germany), H.-J. Chevalier, U. Lafrenz and G. Reckzeh. *Z. Krebsforsch.* 73(3):248-250, 1970.

When 75 Syrian golden hamsters (Group A; age, sex not specified) received a single intratracheal inj. of 9,10-dimethyl-1,2-benzanthracene (500 µg, suspended in a 1% soln. of carboxymethylcellulose in physiologic saline), the number of animals dying after 3, 4, 5, 6, 7, 8 and 9 mo., and the total number of adenomatoid lesions of the lung which were found in each group, were tabulated as follows: 1 and 2, 0 and 0, 2 and 3, 1 and 22, 2 and 4, 16 and 20, 16 and 16, resp. Papillomas of the larynx (1) or trachea (2) were found only in animals of the 6 mo. survival group. Comparable tabulations among 75 animals which received 2 such inj. (Group B; interval not specified) were 7 and 2, 0 and 0, 2 and 0, 16 and 18, 1 and 1, 22 and 30, 13 and 17, resp. Three papillomas of the trachea were found in animals of the 8 mo. survival group. The number of metaplastic lesions of the larynx or trachea were tabulated for each survival period for animals in Group A, as follows: 1, 0, 2, 13, 3, 11 and 8, resp. Comparable tabulations for animals in Group B were 2, 0, 0, 8, 0, 12 and 9, resp. It was concluded that this method may be suitable as a pretreatment technique in attempting to demonstrate weak carcinogenic or cocarcinogenic effects on the respiratory tract.

- 70-208 ON THE BIOCHEMICAL MECHANISM OF TUMORIGENESIS IN MOUSE SKIN. II. EARLY EFFECTS ON THE BIOSYNTHESIS OF NUCLEIC ACIDS INDUCED BY DOSES OF DMBA AND BY PROMOTING DOSES OF PHORBOL-12,13-DIESTER TPA. (E.) Paul, D. (Nat. Polytech. Inst., Mexico City) and E. Hecker. *Z. Krebsforsch.* 73(2):149-163, 1969.

In male and female NMRI mice admin. 7,12-dimethylbenzanthracene (DMBA; 10 µM intragastrically), a pronounced inhibition of both

DNA and RNA syntheses was seen during the first 24 hr., followed by intense stimulation. Maximum RNA inhibition was reached earlier than DNA inhibition, while stimulation peaks were reached at similar times (48 hours after treatment). Following sequential topical applications of phorbol-12,13-diester TPA (0.06 µM), the DMBA induced inhibition of DNA and RNA synthesis was practically eliminated. Maximum stimulation was reached earlier with RNA synthesis than DNA.

- 70-209 METABOLISM OF METOPIRONE AND 3-(1,2,3,4-TETRAHYDRO-1-OXO-2 NAPHTHYL)-PYRIDINE IN RELATION TO DMBA INDUCED ADRENAL NECROSIS. (E.) Jellinck, P. H. (Queen's U., Kingston, Ontario, Canada) and T. Garrett. *Experientia* 25(8):799-800, 1969.

7,12-Dimethylbenzanthracene (DMBA; 30 mg in 1.5 ml sesame oil) was admin. by stomach tube to young female Sprague-Dawley rats (140-180 g) 2 hr. after i.p. inj. (50 mg/ml oil) of metopirone (Su-4885; 2-methyl-1,2-bis-(3-pyridyl)-1-propanone), reduced Su-4885, 3-(1,2,3,4-tetrahydro-1-oxo-2 naphthyl)-pyridine (Su-9055) or reduced Su-9055. The results indicate that comparable doses of the original and reduced forms of metopirone and Su-9055 have about the same effect in preventing adrenal necrosis. Incubation of Su-9055 (0.2 mg) with liver mitochondrial or microsomal fractions and exogenous NADH₂ or NADPH₂ did not produce any of the reduced form; similar treatment of Su-4885 produced significant reduction. The fact that most of the Su-9055 remained unchanged tends to preclude the possibility of protection through the steric similarity of reduced-Su-9055 to 7-hydroxymethyl-12-methylbenzanthracene, the reduced form of DMBA.

- 70-210 EFFECT OF ORAL COPPER SULFATE ON 7,12-DIMETHYLBENZ(a)ANTHRACENE CARCINOGENESIS IN MICE. (E.) Burki, H. R. (Northwestern U. Med. Sch., Chicago, Ill.) and G. T. Okita. *Brit. J. Cancer* 23(3):591-596, 1969.

Copper sulfate (CuSO₄; 50 mg/l Cu; in H₂O) fed ad libitum to 3-6 mo. old C57BL/6J and strain A virgin and pseudopregnant mice did not affect the incidence of ovarian tumors, breast carcinomas and lymphomas induced by 7,12-dimethylbenzanthracene (DMBA; 0.75 mg i.v. alone or followed in 12 days by 0.5 mg i.p.; or 6 skin paintings of 0.5 ml 0.5% soln. in olive oil). However, CuSO₄ appeared to prolong survival, and may have delayed the development of granulosa cell tumors.

- 70-211 THE EFFECT OF 7,12-DIMETHYLBENZ(a)ANTHRACENE ON THE SYNTHESIS OF LACTATE DEHYDROGENASE ISOENZYMES IN HUMAN FIBROBLASTS. (Ger.) Adamiker, D. (U. Vienna Inst. Biol.), H. Altmann, H. Frischauf, G. Kellner and O. H. Scherbaum. *Experientia* 25(6):590-591, 1969.

Fibroblast cultures grown in monolayers were incubated for 20 hrs. with 0.1 µg/ml of 7,12-dimethylbenzanthracene (DMBA) and the LDH isoenzyme evaluated by means of acrylamide gel electrophoresis, densitometry and incorporation of labeled amino acids. Using disc electrophoresis 3 distinct isoenzyme components were separated. This LDH isoenzyme pattern was not changed by DMBA, however, a marked reduction in enzyme activity was noted in the third farthest traveling fraction and a slight reduction in the first. Amino acid incorporation within these 3 isoenzyme bands showed the same trend with the greatest reduction in radioactivity in the third fraction (from 231 ± 24 to 67 ± 14 counts/min.), less in the first (183 ± 21 to 58 ± 12) and no significant change in the second.

70-212 EFFECT OF AGE AND SEX ON THE DEVELOPMENT OF NEOPLASMS IN WISTAR RATS RECEIVING A SINGLE INTRAGASTRIC INSTILLATION OF 7,12-DIMETHYLBENZ(a)-ANTHRACENE. (E.) Meranze, D. R. (Temple U. Sch. Med. Fels Res. Inst., Philadelphia, Pa.), M. Gruenstein and M. B. Shimkin. Int. J. Cancer 4(4):480-486, 1969.

Of 284 Wistar rats (< 2 to 26 weeks old) of both sexes admin. a single intragastric instillation of 7,12-dimethylbenzanthracene (DMBA; 0.5-1.0 mg in baby rats; 15 mg in adults), 136 developed 182 tumors (50% malignant) within 16 mo.; while 8 tumors (4 malignant) were seen in 98 controls. Survival at 12 mo. was 70%, 50% and 20% in controls, DMBA-males and DMBA-females, resp. Breast cancer was sex-limited, occurring most frequently in 6-8-week-old (at time of DMBA admin.) females; fibroadenoma predominated in < 2-week old rats; older rats showed carcinoma and fibroadenoma in equal frequency. One male castrate developed a mammary adenoma. Epidermoid carcinomas and papillomas of the skin were seen in 22.8% of males and 6.7% of females. Leukemias occurred in 9.45% of DMBA rats (males 16.7%, females 4%) compared with 2% of controls. Connective tissue tumors predominated in the younger rats.

70-213 THYROIDITIS IN BUFFALO STRAIN RATS INGESTING 7,12-DIMETHYLBENZ(A) ANTHRACENE. (E.) Reuber, M. D. (NCI Biol. Lab., Bethesda, Md.) and E. L. Glover. Experientia 25(7):753, 1969.

Inbred 12-wk.-old male and female Buffalo strain rats received a diet containing 0.025% 7,12-dimethylbenzanthracene (DMBA) for 12 wk. after which they were sacrificed. Thyroiditis was seen in 6/10 DMBA-females and in 4/10 DMBA-males, but in none of 23 controls. DMBA-females (thyroiditis and nonthyroiditis) gained an average wt. of 37 g, females controls, 80 g; DMBA-males gained 78 g, male controls, 125 g. The degree of thyroiditis did not vary, but male glands weighed more. In females, the protein-bound iodine and total serum iodine values were

slightly higher in DMBA-animals than in controls. Of the 10 cases of thyroiditis, histologically, 1 was mild, 6 moderate, and 3 severe.

70-214 COMPARISON OF THE EFFICACY OF PRE-TREATMENT PROTECTION AGAINST ADRENAL NECROSIS INDUCED BY 7-HYDROXYMETHYL-12-METHYLBENZ(a)ANTHRACENE AND BY 7-METHYL-12-METHYLBENZ(a)ANTHRACENE IN RATS. (E.) Wheatley, D. N. (McArdle Lab. Cancer Res. Med. Ctr., Madison, Wis.) and P. Sims. Biochem. Pharmacol. 18(10):2583-2587, 1969.

Pretreatment of 50 day old Sprague-Dawley female rats with 3-methylcholanthrene (MC; 1 mg) or 1-(p-phenylazophenylazo)-2-naphthol (Sudan III; 1 mg) i.p. in a single dose 24 hr. before a standard, challenge or overdose of 7,12-dimethylbenzanthracene (DMBA; 30 mg by stomach tube; 5 mg i.v.; or 15 mg i.v., resp.) or 7-hydroxymethyl-12-methylbenzanthracene (7-OHM-MBA; 15 mg by stomach tube; 3 mg i.v.; or 7.5 mg i.v. or 30 mg intragastrically, resp.) completely protected the adrenal glands from adrenal necrosis. Varying degrees of protection were seen after pretreatment (i.p. 24 hr. before DMBA or 7-OHM-MBA, as above) with 1-hydroxy-3-methylcholanthrene, p-dimethyl-aminoazobenzene, DMBA, phenobarbital, glutethimide, chlorpromazine, 7-OHM-MBA and 12-OHM-MBA. No protection was seen after admin. of saline, oil or emulsion. The authors concluded the 7-OHM-MBA is not in itself adrenocorticolytic.

70-215 LEIOMYOSARCOMAS INDUCED BY 7,12-DIMETHYLBENZ[a]ANTHRACENE IN GASTRIC CYSTS GRAFTED IN SUBCUTANEOUS TISSUE OF MICE. (E.) Matsuyama, M. (Aichi Cancer Ctr. Res. Inst., Nagoya, Japan) and H. Suzuki. Gann 60(3):333-334, 1969.

Newborn male C57BL/6Ms and dd/I mice were grafted with sheets of the glandular stomach of male littermates; 2 mo. later, 1-2 mg 7,12-dimethylbenzanthracene (DMBA) was inj. into the luminal space of the resulting cysts. Seventy-day survival was seen in 32/44 mice. In the C57BL/6Ms mice, 4 had severe graft-destroying ulceration at the inj. site, while 8 died or were sacrificed in weakness with a large sarcoma at the site of grafting within 128-210 days after inj.; 14/18 dd/I mice developed sarcomas and died within 98-164 days after inj. All sarcomas were histologically leiomyosarcomas, frequently invading the chest wall and pleural cavity, with hematogenous metastasis to lung, liver and spleen in 2. The sarcomas consisted mainly of spindle-shaped cells with scattered large polygonal cells and some mitotic figures. A few thymic and nonthymic lymphomas and lung adenomas were found. Adenocarcinoma could not be produced with the above technique.

70-216 THE EFFECTS OF 7,12-DIMETHYLBENZ(a) ANTHRACENE ON THE OVARIAN RESPONSE OF MICE AND RATS TO GONADOTROPHINS. (E.) Jull, J. W. (U. British Columbia, Vancouver, Canada) and A. J. Phillips. Cancer Res. 29(11):1977-1987, 1969.

Decrease in ovarian wt. was seen after admin. of 7,12-dimethylbenzanthracene (DMBA; 30 mg/100/g) by stomach tube in C57BL/6J, C3D2F₁, CAF₁, B6AF₁, B6D2F₁ and C57BL/6J x C3HeB/FeJ mice, but not in C3HeB/FeJ x NZY mice or Sprague Dawley or Fischer rats. Ovarian wt. gain after chorionic gonadotropin (CG) inj. was eliminated by DMBA admin. in C57 mice 34 days of age or less and C3D2F₁ mice up to 23 d old, but not in older mice of both strains. Ovarian wt. response to CG was reduced by DMBA admin. in mature B6D2F and CAF₁ and immature B6AF₁ mice, but no significant effect was seen in mature B6AF₁, C57BL/6J x C3HeB/FeJ or C3HeB/FeJ x NZY mice. Substitution of pregnant mare serum for CG produced similar results. Uterine wt. was lower in most immature DMBA treated animals and increased less following CG inj.; but DMBA did not seem to affect the majority of mature animals. The number of viable ovarian follicles was greatly reduced in mice, but not rats, after DMBA treatment.

70-217 MECHANISM OF INDUCTION OF OVARIAN TUMORS IN THE MOUSE BY 7,12-DIMETHYLBENZ[a]ANTHRACENE. VI. EFFECT OF NORMAL OVARIAN TISSUE ON TUMOR DEVELOPMENT. (E.) Jull, J. W. (U. British Columbia Cancer Res. Ctr., Vancouver, Canada). J. Nat. Cancer Inst. 42(6):967-972, 1969.

Donor 5-6-wk.-old female (C3HeB/FeJ x NZY)F₁ mice received intragastric instillation of 7,12-dimethylbenzanthracene (DMBA; 5 mg in 0.5 ml arachis oil) 24 hr. before s.c. transplantation of their ovaries to the right and left inguinal regions of ovariectomized isogenic recipient mice. In 45 mice oophorectomized (ooph.) at the time of transplantation, a 56% incidence of granulosa-cell ovarian tumors were seen beginning after 10 weeks. The incidence was 25% when ooph. was delayed 6 weeks, 17% when delayed 12 weeks. No such tumors were seen in any of 29 recipient mice not subjected to ooph. A tumor larger than 5 mm in diameter was seen in 68% of those with immediate ooph. and 20% of those with delayed ooph. Breast acini were seen in 3% of tumorless mice and in 62% of mice retaining one of their ovaries. Another group of mice was bilaterally ooph. 1 wk. before s.c. implantation of DMBA-ovaries, and untreated-ovaries were implanted s.c. in the back of the neck either immediately (tumor incidence 29%; no acini), after 6 wk. (50%, acini in 1/5 tumorless mice) or after 12 wk. (10%; no acini); acini were never seen in tumor-bearing mice. In a third group, DMBA- or untreated ovaries were implanted

in the groins of mature, 4-5-mo.-old female mice who were mated with CNZ males and had 2 litters each suckling for 3 wk. Here tumors were seen only in mice ooph. 22 weeks after start of the experiment (DMBA-, 33%, untreated, 11%).

70-218 MECHANISM OF INDUCTION OF OVARIAN TUMORS IN THE MOUSE BY 7,12-DIMETHYLBENZ[a]ANTHRACENE. V. EFFECT OF METABOLIC INHIBITORS. (E.) Jull, J. W. (U. British Columbia Cancer Res. Ctr., Vancouver, Canada). J. Nat. Cancer Inst. 42(6):961-966, 1969.

Donor (C3HeB/FeJ x NZY)F₁ (CNZ) female 6-12 week old mice were inj. with either metopirone, actinomycin D, aflatoxin B₁, cycloheximide, or ethionine (10 mg, 100 µg, 200 µg, 800 µg and 10 mg, resp.) at a rate of 15 min., 4 hr., 4 hr., 1 hr., and at 4 and 1 hr., resp., prior to i.v. inj. of 7,12-dimethylbenzanthracene (DMBA; 100, 200 or 500 µg). One hour after DMBA inj., donor mice were sacrificed, ovaries decapsulated and implanted s.c. in the groins of oophorectomized 4-8-mo.-old recipient female mice. The incidence of ovarian granulosa-cell tumors found in the grafts 22 weeks later was 20-40% for 500 µg DMBA, 10% at 200 µg, and 20% at 100 µg. The incidence of breast acini increased with increasing doses of DMBA. No significant anti- or cocarcinogenic effects were seen with admin. of metabolic inhibitors (in 100 µg-DMBA mice).

70-219 THE EFFECT OF ENDOCRINE FACTORS ON CALCIFICATION OF MAMMARY TUMORS OF RATS INDUCED BY 7,12-DIMETHYLBENZ(a)ANTHRACENE. (Ger.) Kovács, K. (U. Montreal Inst. Med., Canada) and A. Somogyi. Z. Krebsforsch. 73(2):193-194, 1969.

After inducing mammary tumors in mature 180 g female Sprague Dawley rats by intragastric admin. of 40 mg 7,12-dimethylbenzanthracene (DMBA) groups of animals were treated either with dihydrotachysterol (DHT) alone (2 mg by stomach tube) or followed by bilateral oophorectomy, s.c. inj. of 5 g/day of estradiol, progesterone, testosterone or triamcinolone. Histological examination of tumors 8 days after DHT application showed that the calcium deposits which were present in these tumors were not influenced by these treatments and that there was either no or very slight increase in calcification after DHT. In all cases the intensity of calcification paralleled the extent of necrosis.

70-220 HYDROCARBON-INDUCED LEUKEMIA IN ADOLESCENT AND ADULT MICE. (E.) Uematsu, K. (Osaka U. Med. Sch., Japan) and C. Huggins. Gann 60(5):545-555, 1969.

7,12-Dimethylbenzanthracene (DMBA) admin i.v. in 4 pulse doses (100 mg/kg 4 x at 2-week intervals) to 40 (25-day-old and 40-50-day-old female CF₁ mice induced leukemia in 33/34 (97.1%) 23/28 (82.1%) animals, resp., surviving > 60 days.). First manifestations were detected between 44-138 days in the young and 64-146 days in the adult group (av. 99 and 98 ± 22 resp.). The thymus was the most frequently involved organ (51.5% young, 65.2% adult) lymph nodes in 9.1% and 8.7%, resp., combination of several organs in 36.4% and 21.7%, resp. Lymphocytic leukemia was seen in 75.8% of young and 83.6% adult, myelocytic in 21.2% and 17.4% resp. Small (microscopic) ovarian tumors were detected in 14 (41.2) of young and 6 (21.4%) adult mice; 5 (17.9%) of the latter also had large (> 0.4 cm) ovarian tumors. Mammary tumors were seen in 3 (8.8%) young and 2 (7.1%) adult; lung tumor in 8 (23.5%) and 2 (7.1%), resp., ear carcinoma in one each, skin tumor in 3 (8.8%) of young. Examination of vaginal smears revealed strong inhibition of ovarian function after pulse dose admin. Serial examination of ovaries after 100 mg/kg DMBA inj. (i.v.) (separate experiment) showed degenerative changes or necrosis of both follicles and corpora lutea (occurring earlier in adult than young animals). The volume of cells in peripheral blood was measured using a distribution curve of particles and 2 peaks were obtained: one (63-125 μ^3) represented lymphocytes, the other (190-250 μ^3) granulocytes. It is suggested that the method is useful in classification of types of leukemia.

70-221 CHROMOSOMAL ANALYSIS OF SOME TRANSPLANTED TUMORS INDUCED BY 3-METHYLCHOLANTHRENE IN GOLDEN HAMSTERS. (E.) Popescu, N. C. (Inst. Oncol., Bucharest), L. Cioloca, F. Liciu and I. Encut. Int. J. Cancer 4(6): 785-792, 1969.

Primary tumors obtained by 3-methylcholanthrene inoc. in golden hamsters (latency period, 100-110 days) were allogeneically transplanted. Aneuploid changes appeared in all the originally diploid tumors. In 3 primary tumors the diploid chromosome constitution was lost and they became heteroploid. The presence of host cells was observed in 2 tumor lines and a new tumor cell population occurred with multiple severe chromosomal aberrations in 1 line. No specific chromosomal changes were observed, but chromosomal markers and a nonrandom distribution in some chromosome groups was identified in each line.

70-222 THE EFFECT OF METHYLCHOLANTHRENE ON THE CONTRACTION BEHAVIOR OF MOUSE SKIN. (Ger.) Seilern-Aspang, F. (U. Vienna Inst. Cancer Res.), K. Mazzucco and I. Christian. Europ. J. Cancer 5(3):211-214, 1969.

Eight mo. old GP strain mice received back paintings of methylcholanthrene (MC; 30 applications over 10 weeks) and were compared for

different skin shrinkage properties in relation to age, sex and size of skin strip using 6 week, 8 mo. and 12 mo. old control animals. MC-treated skin showed changes similar to but greater than those seen in aging with these changes being more pronounced in females. Skin contraction temperature increased approx. 3 degrees C above that of controls; the degree of contraction decreased almost 10% and capacity for relaxation after contraction was markedly reduced. The results indicate that MC causes a specific aging process to occur: increased intermolecular linkage of dermal collagen. Another explanation for the increase in contraction temperature might be a change in collagen content with simultaneous hyperplasia of the epidermis.

70-223 DIFFERENCES IN CARCINOMA INDUCTION IN MOUSE TAIL AND BACK SKIN IN RELATION TO ITS CONTRACTION PROPERTIES. (Ger.) Seilern-Aspang, F. (U. Vienna Cancer Res. Inst.), K. Mazzucco and I. Christian. Europ. J. Cancer 5(3):215-217, 1969.

Skin contraction properties were compared in 6 week, 8 mo. and 12 mo. old GP male mice (10 each). In addition, 200 male mice were painted (30 x within 10 weeks) on the tail or back with a 0.5% soln. of methylcholanthrene (MC) dissolved in benzene or with benzene alone. Papillomas developed in 100%, carcinomas in 90% of carcinogen painted backs while no carcinomas or papillomas developed on the tails. The contraction temperature of tail skin was considerably higher, degree of contraction lower and subsequent relaxation ability higher than that of back skin. Treatment of tail skin with MC caused a lesser increase in contraction temperature (1 degree C) than seen with back skin, and, contrary to back skin, did not affect the degree of contraction or subsequent relaxation.

70-224 DIFFERENCES IN MATURATION OF COLLAGEN FROM THE BACK AND TAIL SKIN OF MICE, WITH RESPECT TO THEIR DIFFERENT SUSCEPTIBILITIES TO TUMOR INDUCTION. (Ger.) Mazzucco, K. (U. Vienna Inst. Cancer Res.), F. Seilern-Aspang and I. Christian. Europ. J. Cancer 5(5):491-496, 1969.

Patterns of collagen maturation were studied in back and tail skin from 19-130-day-old male Swiss albino mice. A high percentage of newly synthesized collagen from back skin consisted of an acid-soluble form, which apparently was not a precursor of insoluble collagen. Newly synthesized tail skin collagen consisted predominantly of a cysteamine-extractable form, which apparently favored further cross-linkage. Cross-linkage of collagen was more extensive and more rapid in tail skin than in back skin. The results suggested the formation of a highly cross-linked collagen, relatively resistant to both degradation by collagenase and to the loss

of collagen induced by carcinogen painting in tail skin. It is suggested that the presence of this highly cross-linked collagen in tail skin might explain the insensitivity of the tail skin to methylcholanthrene carcinogenesis, by comparison to the high sensitivity of the back skin.

70-225 SKIN NUCLEIC ACID PHOSPHORUS METABOLISM OF DBA/1J MICE DURING IMPLANTED TUMOR DEVELOPMENT AND METHYLCHOLANTHRENE CARCINOGENESIS. (E.) Scholes, V. E. (North Texas State U., Denton). Cancer Res. 29(7):1416-1419, 1969.

DBA/1J mice (4-6 weeks old) were implanted with a lymphosarcoma (passage 54) derived from a DBA/1J mouse painted with methylcholanthrene (MC) as below. Mice were sacrificed at 2-day intervals, 12 hr. prior to which they were inj. s.c. with 3 μ C of 32 P/g body wt. Within 2 days of implant, the nucleic acid phosphate (NA-P) RSA (a measure of the complete turnover rate) of histologically normal skin from the tumor-bearing mice had doubled over control values, and was 4 times normal by 6 days, the time between implantation and death of the animal. Activity returned to normal within 10 days. Histologically normal skin, taken 5 days after implant from tumor-bearing mice, developed into lymphosarcomas in 30% of hosts when implanted in syngeneic mice; with 6-day skin, the tumor incidence was 68%. Mice were painted on the dorsal unepilated interscapular skin with a soln. containing 0.6% MC in benzene, 5 x/wk x 9 weeks. Epilation occurred after 1 week's painting, papillomas within 6 weeks, and squamous cell carcinomas by 9 weeks. The RSA of NA-P was 4 x normal within 2 weeks, after which it began to decrease, even with continued painting. A marked increase in turnover rate was seen in unpainted ventral skin from these mice. Tumor incidences after implantation of histologically normal ventral skin from painted mice into syngeneic hosts were 15% at 6 weeks, 40% after 9 weeks and 70% after 39 weeks.

70-226 IN VITRO MALIGNANT TRANSFORMATION OF CELLS DERIVED FROM MOUSE PROSTATE IN THE PRESENCE OF 3-METHYLCHOLANTHRENE. (E.) Chen, T. T. (Indiana U. Med. Ctr, Indianapolis) and C. Heidelberger. J. Nat. Cancer Inst. 42(6):915-925, 1969.

The B1 cell line (from C3H ventral prostate) was exposed in culture to 3-methylcholanthrene (MC) in 0.5% dimethyl sulfoxide (DMSO); the percent inhibition of cell growth was 0% with DMSO controls; 0.5 μ g/ml MC 39%; 1.0 μ g/ml MC, 44%; and 2.0 μ g/ml MC, 58%. Cells exposed to MC for 6 days, and then observed in MC-free medium for 0-14 days, were found to pile up in a criss-cross, randomly oriented fashion, compared with untreated cells that remained in monolayer. Transformed MC-cells were fibroblastic, refractile, randomly oriented and stained heavily with Giemsa; controls also showed fibroblastic cells, but

these were smaller, oriented in a more orderly and parallel fashion and stained lightly with Giemsa. The growth rate of MC-transformed cells was twice that of controls. The aneuploid lines not treated with MC eventually reached a saturation density and, after culture for 152 days, did not induce tumors when inj. s.c. into irradiated (400-500 R) C3H adult males. Cell lines derived from transformed colonies did not reach a saturation density and produced malignant fibrosarcomas in 100% of unconditioned mice after s.c. inj. These tumors could be induced when cells were inoc. only 19 days after initial exposure to MC, suggesting that, in this system, in vitro carcinogenesis is produced by MC in the absence of spontaneous malignant transformation.

70-227 ELECTRONIC PROPERTIES OF N-HETERO-AROMATICS. XXXV. FURTHER OBSERVATIONS ON THE CHARGE TRANSFER INTERACTION OF THE CARCINOGEN, 4-NITROQUINOLINE 1-OXIDE, WITH DNA AND DEOXYRIBONUCLEOSIDES: ANALYSIS OF THE VISIBLE DIFFERENCE BANDS. (E.) Okano, T. (Tohoku U. Sch. Med., Sendai, Japan), K. Uekama and E. Taguchi. Gann 60(3):295-305, 1969.

New absorption bands were detected in the visible difference spectra of mixed systems of DNA and the deoxyribonucleosides (dA, dG, dT, dC) with 4-nitroquinoline 1-oxide (NQO); the bands were all of the same character. The component deoxy ribonucleosides complexed with NQO in a 1:1 stoichiometry. The bands observed with similar complexes between 4-nitropyridine 1-oxide and DNA and the deoxyribonucleosides were less intense than those with NQO. From a physico-chemical standpoint, it is suggested that the deoxyribonucleosides may behave as n - and π -donors simultaneously, such that the complexes may have been stabilized by the cooperative forces of charge transfer of both n - π and π - π types, this hypothesis is supported by observed values of ϵ , κ , and ΔH .

70-228 ELECTRONIC PROPERTIES OF N-HETERO-AROMATICS. XXXVI. INTERACTION OF THE CARCINOGENIC 4-NITROQUINOLINE 1-OXIDE WITH PROTEINS AND AROMATIC AMINO ACIDS. (E.) Okano, T. (Tohoku U. Sch. Med., Sendai, Japan), S. Takenaka and Y. Sato. Gann 60(3):307-317, 1969.

Both 4-nitroquinoline 1-oxide (NQO) and 4-nitropyridine 1-oxide (NPO) were found to complex with proteins (bovine pancreatic RNase-A, γ -globulin, chymotrypsinogen-A) and aromatic amino acids (L-tryptophan, L-histidine, L-tyrosine and L-phenylalanine). Physico-chemical observations showed the complexes of NQO and NPO with the amino acids to be of a π - π charge transfer nature. Since neither 1-oxide was ionized at the pH used in the studies, it is quite doubtful that ionic interactions are of any importance in the complexing. Hydrogen bonding probably played a role in the complexing of L-tyrosine.

The characteristics of the spectra of the protein-1-oxide complexes suggest that charge transfer through aromatic amino acid residues is of importance. On the basis of equilibrium dialysis experiments which show the proteins to have the same number of binding sites for NQO and NPO and on the basis of differences in the binding constant, it is concluded that NQO is bound more firmly to protein than is the non-carcinogenic NPO.

70-229 DETECTION OF POTENTIAL WEAK CARCINOGENS AND PROCARCINOGENS. I. EFFECT OF THE DERIVATIVES OF 4-NITROQUINOLINE 1-OXIDE ON SUBMANIFESTATIONAL DOSE OF 4-NITROQUINOLINE 1-OXIDE. (E.) Hoshino, H. (Nat. Cancer Ctr. Res. Inst., Tokyo), Y. Kawazoe and F. Fukuoka. Gann 60(5): 523-527, 1969.

After establishing the submanifestational dose (by application to skin of 40 day old ddN female mice and observation for 430-450 days) of 4-nitroquinoline-1-oxide (NQO; 20 applications of 0.05 mg), 4,7-dinitroquinoline 1-oxide (30, 60 and 150 applications of 0.05 mg) and 3-methyl-4-nitroquinoline 1-oxide (60 applications of 0.25 mg), the additive carcinogenic effect of these submanifestational doses was tested. Twenty applications of NQO when followed by 30 of 4,7-dinitroquinoline 1-oxide resulted in no malignant tumors but when followed by 60, induced malignant tumors in 2/20 after 297-329 days and when followed by 150 applications induced malignant tumors in 4/20 after 258-329 days (2 fibrosarcomas, 1 squamous cell carcinoma, 1 carcinosarcoma) and a benign papilloma in 1/20. NQO followed by 60 applications of 3-methyl-4-nitroquinoline 1-oxide induced malignant tumors in 2/19 (squamous cell carcinoma and carcinoma) after 213-238 days.

70-230 STUDIES ON EARLY EVENTS IN IN VITRO CARCINOGENESIS WITH 4-NITROQUINOLINE 1-OXIDE. I. EFFECT ON MACROMOLECULAR SYNTHESIS AND CELL LIFE CYCLE. (E.) Kuroki, T. (Tohoku U. Cancer Res. Lab., Sendai, Japan), J. Ishizawa and H. Sato. Gann 60(3):261-272, 1969.

The *in vitro* synthesis of DNA and RNA in hamster embryonic cells was inhibited by 4-nitroquinoline 1-oxide (NQO) and 4-hydroxyaminoquinoline 1-oxide (HAQO), but not by the noncarcinogenic 4-aminoquinoline 1-oxide (AQO). Incorporation of labeled precursors was 10-20% of controls in NQO- and 50% in HAQO-treated cells. Protein synthesis was inhibited only by NQO. The overall actions of NQO were characterized by marked inhibition of macromolecular synthesis and block of the cell life cycle from G1-S and from G2-M. HAQO interfered with cells in the S-G2 period. Recovery from HAQO-induced inhibition occurred within 48 hr. No effects on cell cycle or macromolecular synthesis were seen with AQO. It is concluded that HAQO may be nucleic acid-specific.

70-231 MORPHOGENESIS OF EXPERIMENTAL TUMORS OF THE ESOPHAGUS. (E.) Napalkov, N. P. (N. N. Petrov. Res. Inst. Oncol., Lab. Exp. Tumors, Leningrad, USSR) and K. M. Pozharisski J. Nat. Cancer Inst. 42(6):927-940, 1969.

Male noninbred albino rats (100-140 g) were admin. p.o. an oil soln. of N-methyl-N-nitrosoaniline (MNA; total dose; 268.9-1472.2 mg), initially admin. 5-6 X/wk. at 14 mg/kg/day, but this was increased to 28 mg/kg/day after 4-5 mo. Benign tumors were detected after a mean of 390 days, carcinoma after 538 days. The initial changes in the anatomy of the esophagus consisted of acanthosis of the epithelial lining. Compared with untreated controls, MNA-treated mice showed a higher incidence of endophytic growths of the epithelial lining; these were bigger and extended deeper within the lamina propria. Leukoplakic foci resulted from the above and from hyperkeratotic and parakeratotic changes. In the next phase, leukokeratosis resulted from hypertrophy and proliferation of the mucosal papillae in the leukoplakic foci. Mucosal polyps were seen to develop into papillomas, some of which were transformed into carcinoma.

70-232 METABOLISM AND BINDING TO CELLULAR MACROMOLECULES OF A SERIES OF HYDROCARBONS BY MOUSE EMBRYO CELLS IN CULTURE. (E.) Duncan, M. (Chester Beatty Res. Inst., London), P. Brookes and A. Dipple. Int. J. Cancer 4(6): 813-819, 1969.

Eight tritium-labeled carcinogenic and non-carcinogenic polycyclic hydrocarbons were metabolized to water-soluble derivatives by mouse embryo cells at about the same rate when each was added to the medium at a low conc. (0.05 μ M). With much higher conc. (up to 4.0 μ M), the time required for complete metabolism of the hydrocarbons was considerably increased. The extent of binding of hydrocarbon to DNA and RNA in relation to the amount of hydrocarbon metabolized was greater with the carcinogens than the noncarcinogens. Dibenz(a,h)anthracene was an exception in the latter group.

70-233 EARLY DEVELOPMENT OF INJECTION-SITE SARCOMAS IN RATS: A STUDY OF TUMOURS INDUCED BY IRON-DEXTRAN. (E.) Carter, R. L. (Roy. Cancer Hosp., London). Brit. J. Cancer 23(3):559-566, 1969.

Iron dextran (ID; 50 mg/week; i.r.) was admin. to 60 5-8-wk.-old male CB Wistar rats until sacrifice (4-64 weeks after start of the experiment). Control animals received physiological saline. Tumors at the inj. site were confined to rats receiving ID. The first macroscopic sarcoma appeared 31 weeks after beginning of the experiment; the first microscopic sarcoma was seen in 33 wk. In all, 25/60 rats developed local sarcomas (17/25 macroscopic only; 3/25

macro- and microscopic; and 5/25 microscopic only). Av. induction time was 45 wk. Once palpable, tumors grew rapidly and most rats had to be sacrificed within 20-30 days. Macroscopic sarcomas were similar to spindle cell and pleomorphic tumors previously described in ID inj. rats. Microscopic tumors appeared initially as "clear zones" between accumulations of siderophages and were composed of atypical spindle cells in a pool of amorphous ground substance.

70-234 THE IMPORTANCE OF IMPLANTATION SITE IN CEREBRAL CARCINOGENESIS IN RATS. (E.)

Hopewell, J. W. (St. Mary's Hosp. Med. Sch., London) and E. A. Wright. Cancer Res. 29(11): 1927-1931, 1969.

Male and female Sprague Dawley rats received intracerebral superficial (flush with meningeal surface) or deep (3-4 mm into the brain) implants of pellets of 20-methylcholanthrene (3-7 mg) or 3,4-benzpyrene (3-7 mg) at 4-6 weeks of age. All animals were allowed to live to natural death. Tumors developed in 77% of animals with deep implants, and in 11% of superficially implanted animals. All but one tumor in deeply implanted animals were gliomas and these tumors developed earlier in males than in females.

70-235 ENZYME HISTOCHEMICAL AND ENZYME ELECTROPHORETIC STUDIES OF CADMIUM INDUCED SARCOMAS OF THE SKIN IN ALBINO RATS. (Ger.)

Knorre, D. (St. George Hosp., Leipzig, Germany). Z. Krebsforsch. 72(3):254-257, 1969.

Skin tumors (mostly spindle cell sarcomas) were induced in 6/45 mature male Wistar rats (observed for > 7 mo.) after single s.c. inj. of 0.2 ml/100 g body wt. of $\text{CdCl}_2 \cdot 2\text{H}_2\text{O}$ (337 μg /100 g body wt. of Cd). Alkaline phosphatase was present only in the stroma of tumor-specific capillaries, but not in tumor cells. Acid phosphatase and nonspecific esterase generally showed only slight cytoplasmic activity. Of the oxyreductases, succinic dehydrogenase showed weak activity while lactic dehydrogenase and ADH_2 -nitro-BT-reductase showed strong cytoplasmic activity. The strong LDH activity indicated that the terminal product of glycolysis is not in the citric acid cycle but occurs mainly as lactic acid. Agar gel electrophoresis of tumor homogenates revealed 4 isoenzyme fractions in the nonspecific esterase and 3 (3rd, 4th and 5th) in lactic dehydrogenase: the 4th and 5th cathodic (M-enzyme) fractions were the strongest while the 1st and 2nd (H enzyme) anodic fractions were missing. This corresponds to a preponderance of M subunits which are characteristic of anaerobic metabolism.

70-236 THE EFFECT OF PHENOBARBITAL AND HALOGENATED HYDROCARBONS ON NITRO-AMINE CARCINOGENESIS. (Ger.) Kunz, W. (U.

Marburg/Lahn Inst. Pharmacol. Toxicol., Germany), G. Schaude and C. Thomas. Z. Krebsforsch. 72(3):291-304, 1969.

Admin. of diethylnitrosamine (DENA) to 4-week-old 20-25 g NMRI albino mice in drinking water (0.007% conc., 240 mg/kg/day) caused malignant hepatic tumors in 93%, combination of liver and lung tumors in 30%, liver and stomach 37%, stomach alone in 7%. Maximum mortality from tumors occurred in week 26. All animals were dead after 29 weeks. Admin. of phenobarbital (Ph) in water (240 mg/kg/d) in addition to DENA reduced the number of tumors by 20%; liver tumors decreased to 67%, however tumors in stomach increased to 70%. Tumors failed to develop in organs reached after p.o. admin. after passage through liver. Addition of Ph also prolonged survival time by 20%; at week 29, 80% of the mice were still alive. Maximum mortality occurred at 30 weeks and all were dead at 35 weeks. Halothane (H) and methoxyfluorane (Mf) admin. by forced 1 hr./day inhalation (0.7% and 0.4% conc., resp.) did not significantly alter survival time, tumor incidence or localization but caused a change in type of induced tumor. While the ratio of hemangioendothelioma to carcinoma was 26:1 with DENA alone it changed to 2:1 with H and a strong predominance of epitheliomas over hemangioendothelioma was seen with Mf. The total dose of DENA required to cause death varied: 1240 mg/kg for DENA alone, 1330 mg/kg for DENA-Mf (7% increase), 1350 mg/kg for DENA-H (9% increase), and 1490 mg/kg for DENA-Ph (20% increase). It was concluded that the decreased carcinogenic effect of DENA by combination with Ph is caused by its increased degradation resulting from increased activity of hepatic microsomal enzymes induced by Ph. The slight effect obtained by H and Mf is probably due to a predominance of epithelial carcinomas which do not cause early death through hemorrhage.

70-237 TUMORIGENICITY OF ACRIDINE ORANGE.

(E.) Van Duuren, B. L. (New York U. Med. Ctr., N. Y.), A. Sivak, C. Katz and S. Melchionne. Brit. J. Cancer 23(3):587-590, 1969.

Acridine orange (3,6-bisdimethylaminoacridine; AO; 0.85 mg in acetone; applied to the skin 3 times/week) was not carcinogenic for mouse skin nor was it an initiating agent (single application AO followed by repeated phorbol myristate acetate application) when applied to 8 wk. old female ICR/Ha Swiss mice. However, repeated AO application after an initial 7,12-dimethylbenzanthracene (DMBA; 50 μg) dose markedly augmented tumor incidence seen with DMBA alone, but tumors appeared late (322 days to first papillomas). Liver tumors were seen in 3/20 mice after skin application of AO. AO inj. s.c. (0.26 mg and 0.5 mg in tricaprylin) in mice and female Sprague-Dawley rats, resp.,

induced a small number of tumors at the inj. site in both species.

- 70-238 MEDIASTINAL LYMPHOMA IN SWISS MICE RECEIVING URETHAN. VII. KARYOTYPE STUDY OF LEUKEMIC CELLS IN THE BLOOD OF GRAFTED ANIMALS. (Fr.) Cappelaere, P. (Inst. Cancer Res., Lille, France), M. d'Hooghe, L. Adenis and J. Driessens. *C. R. Soc. Biol. (Paris)* 163(7): 1554-1558, 1969.

Newborn Swiss mice received i.p. grafts of a mediastinal lymphoma induced by urethan in hosts of the same strain (passage 175-passage 200) and were sacrificed 8 days later with marked hepatosplenomegaly and extensive lymphadenopathy. In 55.66% of the grafted mice, the mean chromosomal number of the leukemic cells was increased from 40 (controls) to 43, with a range from < 39 (3.33%) to as high as 70-75 (1.5% = hypotetraploid). Only 2% of the treated animals showed the normal chromosomal number of 40; 12% showed 41; 13.33%, 42; 9.33%, 44; 2.66%, 45; 5.3%, between 45-50; 1.5%, between 50-55. In 66/73 mitoses with 43 chromosomes, the additional chromosomes were abnormal, being metacentric instead of telocentric but equal in overall length to the largest telocentric chromosomes. In other instances, the number of abnormal, metacentric chromosomes varied from 1 to 4. In addition, 66% of the mitoses showed the presence of a very large, telocentric chromosome with a marked, secondary constriction at the level of the 2 arms. These anomalies were considered specific for the leukemia, and formed a constant finding in the course of repeated passages.

- 70-239 THE ROLE OF ASCORBIC ACID IN THE PREVENTION OF BLADDER TUMOR FORMATION. (E.) Schlegel, J. U. (Tulane U. Sch. Med., New Orleans, La.), G. E. Pipkin, R. Nishimura and G. N. Schultz. *J. Urol.* 103(2):155-159, 1970.

In 60-120-day-old Swiss albino female mice with cholesterol pellets containing 3-hydroxy-5-carboxy-benzoquinone-(2-hydroxy-6-carboxy-anil)-(1)imide (4) (A), or 3-hydroxyanthranilic acid (3-HOA) implanted in their bladders, 3-HOA was most carcinogenic (9 tumors in 46/70 mice surviving 40 weeks). However, in animals fed ascorbic acid (250 mg%) *ad libitum* in their drinking water, the carcinogenic effect of 3-HOA was the same as cholesterol alone. The authors concluded that 3-HOA itself is not carcinogenic and that an anti-oxidant in the urine in amounts sufficient to prevent oxidation of 3-HOA will also prevent bladder tumor formation beyond that seen in controls. Animals with A implants had the same results as controls.

- 70-240 CYCAD TOXICOSIS IN CHICKENS. (E.) Sanger, V. L. (Michigan State U., East

Lansing) M. G. Yang and O. Mickelsen. *J. Nat. Cancer Inst.* 43(2):391-395, 1969.

In male white Leghorn chickens started at 1 day old on a diet containing cycad-seed kernel or husk (2 or 5% x 14 days; or 0.5 or 1.0% x 28 or 68 weeks), no chickens had tumors attributable to cycads, nor did they have clinical signs of central nervous system disturbances. In the group fed 5% kernel wt. gain was less than in controls, but in other groups wt. did not differ from controls. Liver lesions were no more severe in animals fed 68 weeks than in those fed 28 weeks.

- 70-241 CARCINOGENICITY OF HEATED FATS AND FAT FRACTIONS. (E.) O'Gara, R. W. (NCI Lab. Path., Bethesda, Md.), L. Stewart, J. Brown and W. C. Hueper. *J. Nat. Cancer Inst.* 42(2): 275-287, 1969.

The urea adduct (UA), nonurea adduct (NUA), nonsaponifiable (NS) and volatile fractions of 2 commonly used vegetable fats (fresh and re-used) were tested for carcinogenicity in newborn NIH rats receiving single and multiple doses. S.c. admin. was used for fresh whole corn oil, the UA and NUA of heated corn oil, the NUA's of fresh or heated hydrogenated fat, the NS fraction of fresh or heated corn oil of hydrogenated fat and 2 volatile fractions of heated corn oil. P.o. admin., with or without added benzopyrene (BP) was used for fresh and heated whole hydrogenated fat and fresh corn oil, UA and NUA of heated corn oil and the dregs of heated hydrogenated fat (no BP); i.m. admin. was used with fresh whole corn oil, fresh and heated whole hydrogenated fat, the NUA's of fresh and hydrogenated fat and corn oil and the volatiles of heated corn oil. No tumors developed at the inj. site in 864 mice inj. s.c. with fat or fat fractions. The incidence of lymphosarcoma was zero in those given the NS fraction and 5.5% in those receiving NUA's; the incidence of lymphosarcomas and mammary fibroadenomas was similar to the spontaneous incidence. Marked deformities of the spine or submucosal cysts of the fore-stomach were seen in those inj. s.c. with volatile fractions. Of 17 gastrointestinal neoplasms seen in p.o. fat-fed rats, 10 were in those that also received BP; 30 nonalimentary neoplasms were seen in this group, but none were attributed to fat admin. The induction of sarcomas at the site of i.m. inj. of the NUA's of fresh and heated hydrogenated vegetable fat and corn oil indicates the presence of a carcinogen in these materials. This carcinogenic potential was increased with heating of the fats.

- 70-242 HISTOENZYMATIC STUDIES ON EXPERIMENTAL GLIOBLASTOMAS OF RABBITS. (Ger.) Osske, G. (Med. Acad. Erfurt Path. Inst., Germany), D. Schreiber, J. Schneider and W. Jänisch. *Europ. J. Cancer* 5(5):525-531, 1969.

The occurrence and histochemistry of 11 enzymes in 14 glioblastomas induced by i.v. inj. of N-methyl-N-nitrosourea (MNU; 10 mg/kg every 2 weeks or 20 mg/kg every 4 weeks; total dose 452-655 mg) were studied. Cell and nuclear atypias with a large number of polynuclear giant cells, and hemorrhagic and necrotic foci were the most prominent histological finding. While high acid phosphatase activity was present in all samples, only slight alkaline phosphatase activity was detected in 7/14 tumors. NADH₂ tetrazoliumoxy-reductase and lactate dehydrogenase were found in all samples, especially in the cytoplasm of giant cells; arylesterase was present in 13/14. The lysosomal enzymes, β -D-galactosidase and β -D-glucosidase were present in necrotic and degenerative foci in all but 2 tumors. Adenosine monophosphatase was present in the walls of blood vessels and necrobiotic areas in 8/14, and weak activity of succinic dehydrogenase was detected in 10/14. Glucose-6-phosphatase and cytochrome oxidase activity were not detected. It is stressed that the distribution of enzymes in these tumors, especially of the hydrolytic enzymes, was different from that found in MNU induced nervous system tumors of the rat.

70-243 EFFECT OF UNILATERAL NEPHRECTOMY ON THE DEVELOPMENT OF KIDNEY TUMOR IN RATS TREATED WITH N-NITROSODIMETHYLAMINE. (E.) Ito, N. (Nara Med. U., Japan), Y. Hiasa, A. Tamai and K. Yoshida. Gann 60(3):319-327, 1969.

A higher incidence of renal tumors was seen in male Wistar rats (150-180 g) to whom N-nitrosodimethylamine (DMN; 500 ppm in the diet) was admin. after unilateral nephrectomy (82.7%) than in those given DMN before unilateral nephrectomy (40%), sham-operated before (62.5%) or after (66.7%) DMN, or in non-DMN controls. Unilateral nephrectomy had no effect on the histological nature of the renal tumors. There was a higher incidence of proliferation of tubular epithelium and interstitial infiltration of undifferentiated cells in unilaterally nephrectomized than in sham-operated rats; tumor types included renal cell (4), embryonal cell (28) and hemangio-endothelioma (1).

0-244 HISTOCHEMISTRY OF DIBUTYLNITROSAMINE INDUCED URINARY BLADDER PAPILLOMA IN RATS. (Ger.) Kunze, E. (U. Munich Path. Inst., Germany), A. Schauer and R. Calvoer. Naturwissenschaften 56(12):639, 1969.

Admin. of dibutyl nitrosamine (20 mg/kg/d) in drinking water to female Wistar rats induced urinary bladder papillomas after > 145 days (no other detail). The mucous membrane of these bladder papillomas regularly showed a decrease in alkaline phosphatase activity. The activity of lactate dehydrogenase was decreased irregularly while that of succinic dehydrogenase was always increased. The same changes in enzyme activity

were noted in sharply delineated areas of thickened epithelium even before papilloma proliferation could be detected. Independent of these areas, in other well delineated areas an increase of lactate dehydrogenase was noted. Autoradiographic studies with ³H-thymidine showed a several-fold increase in the labeling indexes in these papillomas. Since most animals died early from extensive esophagus tumors (not specified) no transition of papillomas into carcinoma and no primary bladder carcinomas were observed.

70-245 THE METABOLISM OF 4-ACETAMIDOSTILBENE AND ITS N-HYDROXY DERIVATIVE. (E.) Baldwin, R. W. (U. Nottingham, England) and M. G. Romeril. Brit. J. Cancer 23(3):536-546, 1969.

In adult male Wistar rats admin. ¹⁴C-acetamidostilbene (AAS; 0.67 mg; i.p.) 81% of the radioactivity was excreted in 3 days; preferentially in the urine (55.2% in 24 hr.). Fecal excretion reached a maximum in 48 hr. (39.3%). Metabolites were excreted in the urine mainly as hydroxylated derivatives, either free or as sulphuric and glucosiduronic acid conjugates. N-hydroxy-AAS was the only carcinogenic compound excreted. Fecal metabolites were present mostly as free compounds. Metabolism of N-hydroxy-AAS was similar to that of AAS.

70-246 CARCINOGENIC ACTIVITY OF AMINO-PHENANTHRENES AND THEIR DERIVATIVES. (Ger.) Dannenberg, H. (Max Planck Inst. Biochem., Munich, Germany) and C. Huggins. Z. Krebsforsch. 72(4):321-324, 1969.

Forced feeding of 1, 2, 3 and 9-aminophenanthrene (30, 40 or 50 mg single dose, 50-120 mg total dose) to groups of 50 day old female Sprague Dawley rats caused mammary tumors in all groups 45-125 days later. Tumors developed in 1/5 and 3/5 after 50 and 120 mg resp. of 1-aminophenanthrene, 3/5 after 90 mg of 2-aminophenanthrene, 6/8 after 90 mg of 3-aminophenanthrene and 5/5 after 90 mg of 9-aminophenanthrene. Of the corresponding acetamino-phenanthrenes only the 2-aceto compound resulted in tumors (5/5 after 60 mg). All the free amines and the 3-acetamine were toxic, causing $\frac{1}{2}$ -1 hr. loss of consciousness after application. The 2, 3, and 9 amino-phenanthrene-N-dipropylphosphates showed no carcinogenic activity. Of all the above compounds inj. i.m. into 10-11 week old female CF-1 mice (total dose 2 mg, observation period 250 days) only 3 acetaminophenanthrene caused sarcoma in 1/10. Leukemia was seen in 2/10 animals inj. with 9-acetaminophenanthrene.

70-247 NON-CARCINOGENICITY OF DIMETHYLTHIONITROSAMINE IN RATS. (Ger.) Schmähl, D. (Cancer Res. Ctr., Heidelberg, Germany) and F. W. Krüger. Z. Krebsforsch. 73(2):191-192, 1969.

Dimethylthionitrosamine was inj. s.c. into 30 3-mo.-old BD VIII rats in 13 mg/kg (10% of LD₅₀) dose once/week up to a total dose of 1196 mg/kg. Only 1/30 developed a malignant seminoma-resembling tumor after 69 weeks and 897 mg/kg. No hepatic damage was seen. For comparison 30 rats of the same strain were inj. s.c. with an equitoxic dose (4 mg/kg once/week up to 360 mg/kg) of dimethylnitrosamine. In this group 8/30 developed hepatocellular carcinomas, 2/30 hemangio-endothelioma of the liver, 1 hemangiosarcoma of small intestines, 1 mammary carcinoma and 1 fibrosarcoma. Since in dimethylthionitrosamine a sulfur atom is substituted for oxygen in the dimethylnitrosamine molecule it is concluded that sulfur abolishes the carcinogenic activity of simple nitrosamines.

70-248 CARCINOGENIC ACTION OF N-NITROSODIBUTYL-AMINE IN MICE. (E.) Takayama, S. (Cancer Inst., Tokyo) and T. Imaizumi. Gann 60(3):353, 1969.

A diet containing 50 ppm N-nitrosodibutylamine (NDBA) was fed to male ICR mice for 12 mo. Twelve-mo. survival was seen in 33/39. In the 33, squamous cell carcinoma of the forestomach was seen in 27, squamous papilloma in 6, with lung and node metastasis in 2; esophageal papilloma was seen in 4; trabecular hepatoma in 5, liver adenoma in 10; lung adenoma was seen in 8; marked splenic amyloidosis in 7. Fifteen-mo. survival was seen in 28/30 non-NDBA controls, 2 of whom had lung adenoma and one lymphatic leukemia.

70-249 DYSOONTOGENETIC SKIN TUMOURS IN PIGLETS INDUCED BY TRANSPLACENTAL ACTION OF ETHYLNITROSOUREA. (Ger.) Kupfer, M. (Emilienstr. 14, Leipzig, Germany) G. Kupfer, I. Zintzsch, H. Juhls and W. Ehrentaut. Arch. Geschwulstforsch. 34(1):25-33, 1969.

Evaluation of 17 piglets from 2 litters whose mothers received 6 i.v. inj. of N-ethyl-N-nitrosourea (ENU; 20 mg/kg every 2 days between 20-32 days of pregnancy showed adenomas of sweat glands in 11, skin papillomas in 7 (combination of both in 5) in addition to cystic malformations of other organs. Increase in size of some tumors was noted during a several week survival time. Two animals had papillomas on the mucous membrane of the oral cavity. Histological findings are described in detail and it is stressed that undifferentiated epithelium is the matrix of sweat gland adenomas, papillomas and combined hamartomas. In addition to its teratogenic effect, a carcinogenic effect has to be considered for ENU. It should be kept in mind that the observation period considered here was too short to prove definite neoplastic transformation of these skin tumors.

70-250 BIOCHEMICAL, PATHOLOGICAL, AND GENETIC ASPECTS OF A SPONTANEOUS MOUSE HEPATOMA. (E.) Hancock, R. L. (Jackson Lab., Bar Harbor, Me.) and M. M. Dickie. J. Nat. Cancer Inst. 43(2):407-415, 1969.

The incidence of spontaneous hepatomas was 100% by 17 mo. in male (DBA/2Wyd x CE/J)_{F1} mice fed a high fat (11%) diet. Many animals had hepatomas at 6 mo.; and 68% of the males had hepatomas at 1 yr. Females eventually developed hepatomas, but at a much slower rate than males. Great heterogeneity among individual hepatomas was seen in chromosome studies. The hypermethylation phenomena were not seen. In genetic studies, DBA/1J, DBA/2J, and C3H/He hybrids crossed with CE/J mice also had high hepatoma incidence.

70-251 A NEW CARCINOGEN, 2-NITROQUINOLINE: INDUCTION OF LUNG CANCER IN MICE. (E.) Mori, K., M. Kondo (Showa U. Sch. Med., Tokyo), M. Tamura, H. Ichimura and A. Ohta. Gann 60(5):609-610, 1969.

Fifteen female, 5-week-old ICR mice were inj. s.c. with 0.25-1.0 mg of 2-nitroquinoline (dissolved in 0.1-0.2 ml of 10% aqueous soln. of lecithin) in 10 day intervals up to a total dose of 17 mg/mouse. Nine animals survived > 274 days; of these, lung tumor was found in 4/9, carcinoma in 3/9 and adenoma in 1/9. In addition, 3 mice had ovarian cysts and 3 a hypertrophic thymus. No malignant changes were seen at the site of inj. It was concluded that the N-oxide group is not always essential for carcinogenesis, however, it remains to be clarified whether this compound acts through its reduced form, 2-hydroxyaminoquinoline.

70-252 COMPARATIVE CARCINOGENICITY OF N-ISOPROPYL- α -(2-METHYLHYDRAZINO)-p-TOLUAMIDE·HCl (PROCARBAZINE HYDROCHLORIDE), ITS DEGRADATION PRODUCTS, OTHER HYDRAZINES, AND ISONICOTINIC ACID HYDRAZIDE. (E.) Kelly, M. G., R. W. O'Gara (NCI Lab. Path., Bethesda, Md.), S. T. Yancey, K. Gadekar, C. Botkin and V. T. Oliverio. J. Nat. Cancer Inst. 42(2):337-344, 1969.

Ibenzmethylin (IMTH; procarbazine) and 6 other hydrazines were admin. for 8 weeks (1 dose/week; i.p. in males; p.o. in females) to CDF₁ mice. IMTH induced alveolar lung carcinomas in 80-100% of animals treated by either route. The only other hydrazine which increased lung tumor incidence above the control level was hydrazine sulfate (HS), which induced lung tumors in 20-46%. In mice treated p.o. or i.p. with IMTH, leukemias developed in 62% and 48%, resp., after latent periods of 21 and 20 weeks. HS and the other hydrazines did not induce leukemia. In

another group of mice treated p.o. for 8 weeks (1 dose/week of 300 mg/kg) with IMTH or its degradation products, the lung tumor development rates were about the same with IMTH and its hydrazone degradation product (82% and 67%, resp.). The aldehyde degradation product was essentially inactive, the acid degradation product was weakly active, and isonicotinic acid hydrazide (INH) had low activity. In a comparison of p.o. admin. (0.01 ml of 0.5% soln. once weekly x 8) IMTH and its initial oxidative degradation product, N-isopropyl- α -(2-methylazo)-p-tolamide (AZO), were found the following data: pulmonary tumor incidence, 70% for IMTH, 95.2% for its derivative; mean latent period, 25 and 53 weeks; mean nodule count, 5.6 and 8.0, resp. Leukemia was seen with both IMTH and AZO (40% with mean latency 25 weeks, and 14.3% with mean latency of 32 weeks, resp.). Renal cystadenoma was also seen with both IMTH and AZO (20% and 33%, resp.).

70-253 INDUCTION OF BRAIN AND SPINAL CORD TUMORS IN RABBITS WITH N-METHYL-N-NITROSOUREA (MNU). (Ger.) Schreiber, D. (Med. Acad., Erfurt, Germany), W. Jänisch, R. Warzok and H. Tausch. Z. Ges. Exp. Med. 150(1):76-86, 1969.

Of 64 rabbits inj. i.v. with N-methyl-N-nitrosourea (MNU; 10 mg/kg every 2 weeks, group A, or 20 mg/kg every 4 weeks, group B), 27/36 animals admin. the lower dose and 21/28 admin. the higher dose survived a minimum of 194 days (the time at which the first tumor developed). Tumors of the central nervous system (CNS) developed in 19/27 of group A after a minimum of 15 and a max. of 25 inj. and in 14/21 of group B after a minimum of 10 and a max. of 16 inj. These included 19 brain tumors and 2 spinal cord tumors in group A (16 gliomas, 5 sarcomas) and 15 and 2, resp., in group B (4 gliomas, 12 sarcomas, 1 unclassified). Tumors appeared 197-435 days (av. 10 mo.) after the start of the experiment. No tumors of intraspinal or intracranial nerve roots or peripheral nerves were found. Malignant extraneural tumors were present in 25 of the total 48 animals with CNS tumors, 16/48 developed carcinomas of the small intestine, (4/27 of A, 12/21 of B), 15/48 had multiple vessel sarcomas or sarcomatosis of different organs (6/27 of A, 9/21 of B). A combination of CNS and extraneural tumors was detected in 5/27 of A and 12/21 of B animals. Carcinomas at the site of inj. were seen in 4/48 rabbits. It is stressed that i.v. inj. of MNU is the best method for induction of CNS neoplasms in adult rabbits.

70-254 MORPHOLOGY AND HISTOCHEMISTRY OF EXPERIMENTAL BRAIN TUMORS IN RABBITS. (Ger.) Stavrou, D. (U. Munich Inst. Oncol., Germany). Z. Krebsforsch. 73(2):98-109, 1969.

N-methyl-N-nitrosourea inj. i.v. in 10 mg/kg dose every 14 days into 40 3-mo.-old chinchilla

rabbits caused 75% to develop brain tumors (surviving more than 1/3 of induction time) after an av. latency of 268 days (210-349). Av. total dose was 660 mg (480-750). The tumors were classified as oligodendrogliomas I and II (6), polymorph-gliomas (2), ependymoblastoma (1), atypic ependymomas (9) and primary heteromorph gliomas (mixed gliomas). In addition to these macroscopic tumors many unclassified foci-forming "microtumors" were detected. The tumors were located mainly within the subependymal paraventricular areas (especially the lateral ventricles). Enzyme histochemical analysis revealed strong activity of polyphosphatases and anaerobic transhydrogenases, low to moderate activity of glycosidases (especially aerobic transhydrogenases) and slight, irregular activity of L-leucinaminopeptidase. The strongest activity of alkaline phosphatase was seen in tumor capillaries of gliomas, while ependymoma tumor cells also showed moderate activity. Naphthol AS-esterase and lactate dehydrogenase activity was most pronounced in giant cell and strongly anaplastic formations; proliferating capillaries showed strong activity of oxidative enzymes. It is suggested that these results generally correlate with those described for human brain tumors.

70-255 3,4-BENZOPYRENE POLLUTION OF THE ATMOSPHERE IN SHOPS OF THE KRIVOY-ROG BY-PRODUCT COKE PLANT. (Rus.) Petrova, N. V. (Gor'kii Sci. Res. Inst. Industrial Hygiene and Occupational Dis., Moscow). Gig. Tr. Prof. Zabol. 13(10):45-46, 1969.

70-256 NUCLEAR CHANGES PRODUCED BY BLEOMYCIN IN THE 3-METHYLCHOLANTHRENE-INDUCED MOUSE EPIDERMAL CARCINOMA CELLS. (E.) Ogawa, K. (Sapporo Med. Col., Japan) and T. Onoé. Gann 60(5):503-507, 1969.

70-257 DIFFERENT SUSCEPTIBILITIES OF CHICK EMBRYO LIVER CELLS IN VITRO TO AFLATOXIN, ACTINOMYCIN D, AND MITOMYCIN C. (E.) Terao, K. (Chiba U. Inst. Food Microbiol., Japan) and K. Miyaki. Z. Krebsforsch. 71(3):199-207, 1968.

70-258 TISSUE CULTURE OF KIDNEY TUMORS INDUCED BY CYCASIN IN RATS WITH SPECIAL REFERENCE TO WILM'S TUMOR. (Jap.) Shimizu, M. (Gifu U. Sch. Med., Japan). Acta Sch. Med. Gifu 17(1):35-49, 1969.

70-259 FREE RADICAL REACTION OF 4-NITRO-QUINOLINE 1-OXIDE: FORMATION OF 3,3'-(4,4'-DIHYDROXY)BIQUINOLINE. (E.) Kosuge, T. (Shizuoka Coll. Pharm., Japan), H. Zenda, H. Sawanishi and Y. Suzuki. Chem. Pharm. Bull. (Tokyo) 17(10):2178-2181, 1969.

See also abstract nos.: 161,170,303,325,349

70-260 CONTINUOUS VIRAL MULTIPLICATION AND NEOPLASTIC TRANSFORMATION IN CELL LINES ESTABLISHED FROM SPLEEN OF MICE WITH RAUSCHER LEUKEMIA. (E.) Miyoshi, I. (Okayama U. Med. Sch., Japan), T. Tsubota, T. Nagao, H. Takata, S. Irino and K. Hiraki. Gann 60(5): 583-590, 1969.

Splenic tissue from 2 BALB/c mice with Rauscher leukemia gave rise to 2 tissue culture cell lines OUMS-1 and OUMS-2. The growth pattern and morphological features of both were similar for the first 5 mo. of cultivation. The OUMS-1 contained many cells resembling basophilic and orthochromatic erythroblasts, while the OUMS-2 cells later altered into spindle-shaped cells which grew in criss-cross multilayers, indicating neoplastic transformation. Supernatant fluid from OUMS-1 (0.2 ml) caused typical Rauscher leukemia with hepatosplenomegaly when inj. i.p. into 1-4-day-old AKR and BALB/c mice (after 20-35 and 68-88 days, resp.). The supernatant from OUMS-2 culture caused leukemia only in BALB/c (4/7 after 83 days) but not in AKR mice. A reduction of leukemogenic activity was noted after prolonged cultivation. Implantation (i.p. or s.c.) of the transformed OUMS-2 tissue culture cells into 1-4-day-old BALB/c and AKR or 3-mo.-old BALB/c mice resulted in spindle cell sarcomas at site of inoc. after 12-26 days. Cell free extracts of these OUMS-2 derived transplantable tumors were less leukomogenic, causing leukemia in 1/7 and 2/8 BALB/c mice after 113 and 102 days, resp. Electron microscopy revealed many type C particles in the OUMS-1 cell line, substantially fewer in the OUMS-2 cell line and only a few in the OUMS-2 transplantable tumors.

70-261 PLATELET METABOLISM IN RAUSCHER VIRUS LEUKEMIA. (E.) Brodsky, I. (Hahnemann Med. Coll. Hosp., Philadelphia, Pa.) and N. V. Dimitrov. J. Nat. Cancer Inst. 43(2):385-390, 1969.

A decreased platelet count was seen 3 days after infection with Rauscher leukemia virus (RLV; 0.2 ml of 10^{-1} dilution; i.v. in tail vein) in splenectomized (splx; 4 wk. before infection) and nonsplenectomized (non-splx.) weanling female BALB/c mice; the nadir was reached at 14 days after infection in both groups. A sharp increase in CO_2 production was seen in the platelets of non-splx. mice 4 days after infection. Glutamic, and aspartic acids and alanine were identified in the platelets. Total utilization of acetate- $2-^{14}C$ was greater than in controls. Severe thrombocytopenia was present 2 weeks after infection in both non-splx. and splx. mice; but was more severe in splx. No significant changes in coagulation were noted between experimental and control groups.

70-262 IMMUNOSUPPRESSIVE EFFECTS OF LEUKEMIA VIRUSES. STUDIES WITH RAUSCHER VIRUS IN MICE RESISTANT TO LEUKEMIA. (Ger.) Seidel, H. J. (Inst. Exp. Path., Wuppertal-Elberfeld, Germany) and K. Lauenstein. Z. Krebsforsch. 72(3):219-225, 1969.

BALB/c mice (18-22 g, both sexes) and C57/Bl/6 mice (20-23 g, both sexes) were infected i.p. with Rauscher virus (0.2 ml of 10% cell free homogenate of leukemic spleens). Viremia was determined 0, 3, 5, 7, 13 days and in C57/Bl/6 mice also 140 days later. The immunosuppressive effect was determined by titration of hetero-hemagglutinins 7 days after i.v. immunization with heterologous sheep erythrocytes (2.5×10^8 cells) which took place either 2 days before or 3, 7, and 13 days after virus infection (with C57/Bl/6 also 20 and 40 days after infection). BALB/c mice developed typical leukemia, spleen enlargement (> 2 g after 20 days) and viremia which was present already on day 3 and steadily increased. Marked immunosuppression (no antibody formation) was noted when antigen was admin. 7 and 13 days after virus infection. The C57/Bl/6 mice were resistant to leukemia, splenic enlargement was slight (av. wt. 310 ± 70 mg), viremia transitory (3-13 days after infection) and immunosuppression (2-4 fold decrease in titer) demonstrable only when antigen was admin. during the viremic phase (7-13 days). No correlation between size of spleen and immunosuppression could be demonstrated. Since these mice developed viremia but no leukemia it is concluded that immunosuppression is due to a functional disturbance of the immune system caused by the virus and is independent of leukemogenesis.

70-263 TITRATION OF THE LEUKEMOGENIC AND IMMUNOGENIC ACTIVITY OF GRAFFI MOUSE LEUKEMIA VIRUS. (Ger.) Fey, F. (German Acad. Sci. Inst. Cancer Res., Berlin) and G. Pasternak. Z. Krebsforsch. 72(4):356-360, 1969.

Leukemogenic activity was determined by s.c. inj. of 0.1 ml of cell-free filtrates (from XVII/Blm mice with Graffi myeloid leukemia) in 10^{-1} to 10^{-6} dilution into newborn XVII/Blm mice. The highest concentration caused leukemia in 75% of animals, the lowest in 5%. The 50% effective dose was $10^{-3.14}$. The latent period ranged from 138 days for the highest to 304 days for the lowest conc. Approx. 80% of the leukemias were of the myeloid type, and a large proportion of these were chloroleukemias. The median latent period was inversely related to dose of inj. virus. The immunogenic activity was investigated by the antibody production (MAP) test: the same virus preparations were inj. i.p. into adult XVII/Blm mice and antibody

determined (indirect immunofluorescence technique) at weekly intervals. Their presence could be detected already 14 days after inj. of the highest conc. and after 5 weeks in animals inj. with 10^{-5} dilution. The 10^{-6} usually did not induce antibody production. Latency for antibody production was inversely related to virus dose. Although the leukemia induction assay seemed somewhat more sensitive (dilution 10^{-6}) the MAP test was faster giving results after a few weeks as opposed to 4-10 mo. with the former test. It is concluded that both correlate and supplement each other but measure different virus activities.

70-264 LEUKEMOGENESIS INDUCED IN XVIIInc MICE BY ACELLULAR PREPARATIONS DERIVED FROM AN EXPERIMENTAL CHLOROMA. (Fr.) Chamorro, A. (Inst. Radium Pasteur Lab., Paris). C. R. Soc. Biol. (Paris) 163(7):1482-1484, 1969.

Of 68 infant XVIIInc mice inoc. i.p. with 0.1 ml of a chloroma extract containing both Friend's and a myeloid leukemia virus, 10/29 long survivors developed typical or atypical Friend's leukemia while 5/29 developed myeloid leukemia; of 59 mice inoc. with a comparable dose of a cell-free ascitic chloroma cell extract, results were 6/29 and 3/29, resp. Using 49 mice inoc. with a comparable dose of the supernatant of an ascitic chloroma, results were 4/29 and 13/29, resp; a comparable dose of supernatant extract admin. to 84 mice, resulted in 4/36 and 9/36, resp. The latency periods for Friend's and myeloid leukemia were 167-456 and 230-349 days, resp. Extracts of solid and ascitic chloroma cells both induced a 66% take of Friend's leukemia while the ascitic chloroma supernatant and the extract of the same induced a 70 and a 76% take, resp. (for myeloid and chloroleukemias). Compared to previous studies, it is concluded that XVIIInc mice are less susceptible to the leukemogenic complex but more susceptible to the chloroleukemia agent (44 and 26%, total takes, resp.) as contrasted to 63% and 10.6%, resp., for Swiss mice.

70-265 INHIBITION OF FRIEND LEUKEMIA VIRUS SPLENOMEGALY BY AN ACETYLENIC CARBAMATE. (E.) DeLong, D. C. (Eli Lilly Co., Indianapolis, Ind.), L. A. Baker, N. R. Easton and R. D. Dillard. Proc. Soc. Exp. Biol. Med. 127(3): 845-849, 1968.

DBA/2 mice received 1-(4-fluorophenyl)-1-phenyl-2-propynyl N-cyclohexylcarbamate (FPPC; 20 or 30 mg/kg/dose) at 24 and 4 hr. before and 24 and 48 hr. after i.p. infection with Friend leukemia virus (FLV). Spleen wt. in FPPC-treated mice were only 1-2 times that of uninfected controls compared with a 30-fold increase in virus-controls. A plot of mean spleen wt. versus virus dilution revealed a 3-log decrease in virus/unit wet tissue, due to drug treatment, and this was further amplified by the increased wt. of virus-control spleens. A plot of serum virus versus

spleen wt. revealed a 1.7-log decrease in virus. P.O. admin. and i.v. inj. of FPPC were equally effective.

70-266 PROPERTIES OF A VERY ACTIVE INHIBITOR OF MOUSE LEUKEMIA VIRUSES. (Fr.)

Reynaud, M. (Pasteur Inst., Garches, France), J.-C. Chermann, C. Jasmin and G. Mathé. C. R. Acad. Sci. [D] (Paris) 270(3):578-580, 1970.

Single doses (10-5000 µg) of a substance derived from cultures of JLSV-5 cells (normal spleen cells of mice of an unspecified strain, infected with Rauscher virus) were inoc. i.p. into 2-3-mo. old BALB/c mice at periods varying from 4 days before to 8 days after inj. of Friend leukemia virus (20-100 SD₅₀, single i.p. dose), admin. 21 days prior to sacrifice. When inoc. 4 days prior to Friend virus, the substance afforded 100% protection at a dose level of 10 µg/animal; when inoc. 8 days after the virus, it was entirely ineffective at the highest dose level employed. The molecular wt. of the inhibitor was approx. 60,000; the absorption spectrum was max. at 260 mµ. The inhibitor's activity was not affected by DNase, was diminished by RNase, and was destroyed by a proteolytic enzyme (pronase). It showed none of the effects of interferon against the virus of vesicular stomatitis and no activity as an inducer of interferon. The inhibitor was also demonstrable in the spleen of normal mice, possessing the same degree of activity, when extracted, as that possessed by the substance derived from cell cultures. Procedures for deriving the substance from cell cultures are detailed.

70-267 FURTHER STUDIES ON THE ESTABLISHED CELL LINE (AICHI-4) DERIVED FROM A PATIENT WITH HODGKIN'S DISEASE. (E.) Shiratori, O. (Aichi Cancer Ctr. Res. Inst., Nagoya, Japan), Y. Ito, T. Takahashi and Y. Imaeda. Gann Monogr. 7:183-190, 1969.

Positive immunofluorescence (IF+) was detected only when antiserum from a pt. with Hodgkin's disease was matched with AICHI-4 cells. A great increase in the IF+ cells was seen when AICHI-4 cells were incubated at 32°C for 6 days. Morphological changes were seen in 2/5 human embryonic cell cultures treated with cell-free supernatant from AICHI-4 cultures. Rounded cell foci were formed approximately 3 weeks after exposure, and the number of rounded cells forming the focus increased with time. Eventually the cells showed a tendency to disintegrate from the focus. It is suggested that AICHI-4 cells exhibiting a great increase in IF+ cells (incubated at 32°C, 6 days) may harbor the viral agent. This is based on preliminary tests with P3HR-1 cells (high EB virus content) which showed high IF+ cells incubated under conditions as above.

70-268 INFECTIOUS BUT NON-LEUKEMOGENIC FRIEND LEUKEMIA VIRUS OBTAINED AFTER PROLONGED CULTIVATION IN VITRO. (E.) Yoshikura,

H. (Inst. Radium, Orsay, France), Y. Hirokawa, Y. Ikawa and H. Sugano. Int. J. Cancer 4(5): 636-640, 1969.

Cell lines persistently infected with Friend leukemia virus (FLV) were obtained by infection of MLg cells (lung tissue of ddY neonates) at the 65th (MLg65FV56) and 42nd (MLg42FV131) subcultures. The virus produced by MLg65FV56 cells was nonleukemogenic but interfered with Moloney sarcoma virus (MSV) *in vitro* and was also seen to be a helper of defective MSV. The leukemogenicity of the highly leukemogenic virus produced in MLg42FV131 cells was markedly attenuated by *in vitro* cultivation for 1 yr., but the interfering capacity of early passage and attenuated FLV131 was approx. equal.

70-269 ABSENCE OF GROWTH STIMULATION IN CHICK EMBRYO CELLS INFECTED WITH AVIAN LYMPHOMATOSIS VIRUS RAV-1. (Fr.) Biquard, J.-M. (Inst. Radium, Orsay, France). C. R. Acad. Sci. [D] (Paris) 270(2):440-443, 1970.

Fibroblasts derived from Leghorn chick embryos were grown on medium M 199 or on Eagle's medium MEM + a double conc. of vitamins and both essential and nonessential amino acids + 10% tryptose phosphate and varying conc. of calf serum and insulin. Twenty-four-hr.-old cultures were infected with 0.2 ml medium containing 0.1-10.0 infectious units of RAV-1 avian lymphomatosis virus and were then incubated with 5 ml medium for 1-10 days. Irrespective of the calf serum content or the frequency of its renewal, there was no significant difference between control and test cultures with respect to cell growth. The addition of insulin or dextran sulfate to the medium also failed to affect growth; growth was also not affected by the conc. of virus or the duration of incubation. However, when Bryan-strain Rous virus B-RSV(RAV-1) or Schmidt-Ruppin strain Rous virus (SR-RSV) (2 FFU/cell and 1 FFU/cell, resp.) were employed in a series of parallel experiments, the number of cells in infected cultures exceeded the number in control cultures by 50%, from day 2 on. It is concluded that the changes in cell growth induced by B-RSV(RAV-1) are due only to the presence of the Rous virus.

70-270 ENHANCEMENT OF MURINE SARCOMA VIRUS (MOLONEY) INFECTION AND TUMORIGENESIS *IN VIVO* BY COINFECTION WITH RAUSCHER LEUKEMIA VIRUS. (E.) Turner, W. (NCI, Bethesda, Md.) and M. A. Chirigos. Cancer Res. 29(11):1956-1960, 1969.

Adult male BALB/c mice inoc. i.p. with Rauscher leukemia virus (RLV) 5 days before, simultaneously with or 6 days after i.m. inoc. with murine sarcoma virus (Moloney; MSV) had a 93.3-100% death rate from tumors as compared to 13.3% in animals receiving MSV alone. RLV-mediated enhancement was seen throughout the dose ranges

used and was independent of time of challenge. The level of MSV enhancement was maintained over 4 cell-free passages by MSV derived from tumors induced in dually-infected animals.

70-271 IMMUNOLOGIC CHARACTERIZATION OF SARCOMAS ARTIFICIALLY INFECTED WITH THE GRAFFI-LEUKEMIA VIRUS. II. STUDIES ON THE DIFFERENTIATION OF VIRAL AND NEW CELLULAR ANTIGENS. (Ger.) Pasternak, L. (German Acad. Sci. Inst. Cancer Res., Berlin) and G. Pasternak. Arch. Geschwulstforsch. 32(4):301-308, 1968.

Absorption of Graffi mouse immune sera (containing Graffi virus neutralizing antibodies and antibodies against specific surface antigens of leukemia cells) with sediments from homogenates of sarcomas infected with Graffi virus caused a loss of virus neutralizing antibodies. The antibodies reacting with the specific antigens localized on the membrane of leukemia cells (as determined by the indirect immunofluorescence test) remained in the serum. The results confirmed previously reported data indicating that Graffi immune sera contain antibodies against at least 2 different antigenic specificities - viral antigens and new cellular antigens of leukemic cells.

70-272 THE INHIBITION BY CYTOSINE ARABINOSIDE OF THE REPLICATION OF MURINE LEUKEMIA AND SARCOMA VIRUSES IN MOUSE EMBRYO CULTURES. (E.) Hirschman, S. Z. (NCI, Bethesda, Md.), P. J. Fischinger and T. E. O'Connor. Int. J. Cancer 4(5):671-677, 1969.

The growth of mouse Moloney sarcoma virus (MSV) and Rauscher leukemia virus (RLV) in mouse embryo (ME) cultures was inhibited in the presence of cytosine arabinoside (Ara-C; 10^{-5} - 10^{-4} M). Ara-C inhibited the replication of both the competent and defective states of MSV. Despite a 7-hr. exposure to Ara-C, the inhibition of DNA synthesis in MSV-infected cells was reversed by removal of Ara-C. Ara-C failed to affect the growth of vesicular stomatitis virus in ME cultures.

70-273 PATHOGENICITY OF ROUS SARCOMA VIRUS IN TRANSCAUCASIAN HAMSTERS. (Rus.) Zil'fian, V. N. (Armenian Inst. Roentg. Oncol., Erevan, USSR), B. S. Fichidzhian and V. A. Kumkumadzhian. Zh. Eksp. Klin. Med. 7(6):19-23, 1967.

In 5-mo.-old Transcaucasian hamsters (Mesocricetus brandti; both sexes), i.m. inoc. of the Schmidt-Ruppin strain of Rous sarcoma virus (RSV) induced tumors within 20-45 days in 32/36 animals. No tumor regression was noted; the tumor-bearing animals died 60-130 days after RSV inoc. The tumors were identified as spindle cell sarcomas and had the same karyotype as normal hamster

cells. It is concluded that the Transcaucasian hamster is a suitable animal for studies of RSV.

70-274 ROUS SARCOMA VIRUS PRODUCTION IN MIXED CULTURES OF MAMMALIAN ROUS SARCOMA CELLS AND CHICK EMBRYO CELLS. (E.) Yamaguchi, N. (U. Tokyo Inst. Med. Sci.), M. Takeuchi and T. Yamamoto. Int. J. Cancer 4(5):678-689, 1969.

Three mammalian Rous sarcoma cell lines, which were unable to induce infectious Rous sarcoma virus (RSV) by co-cultivation with chick embryo (CE) cells, induced production of RSV when fusion with CE cells was induced by UV inactivated hemagglutinating virus of Japan (UV-HVJ). Infectivity was increased when the UV-HVJ was pretreated with anti-HVJ serum. Because of the presence of RSV genome at every cell level of the parent ascites cell line, SR-C3H/He ascites, and because of the tumorigenic activity of 13 clonal sublines of SR-C3H-2127, it was concluded that most or all of the SR-C3H-2127 cells possess the RSV genome. However, most of the heterokaryons of the Rous sarcoma and CE cells failed to register as infective centers, suggesting that possibly only a small fraction of the heterokaryon population can produce infectious RSV.

70-275 MALIGNANT TRANSFORMATION OF AN ESTABLISHED KIDNEY CELL LINE FROM AFRICAN GREEN MONKEY BY THE SCHMIDT-RUPPIN STRAIN OF ROUS SARCOMA VIRUS. (E.) Sakiyama, H. (Chiba U. Sch. Med., Japan). Gann 60(5):591-594, 1969.

Established African green monkey kidney cells (Vero cells) were co-cultivated with 1.9×10^6 Rous sarcoma cells (from a Rous sarcoma in chick wing web). Morphological transformation of the Vero cells was observed 60 days later. These transformed cells (Vero-R-1 cells) when inoc. ($8 \times 10^5 - 8 \times 10^6$) into white Leghorn chicks < 2 weeks old induced tumors in 11/35 birds. RSV was recovered from these tumors. The tumor-inducing capacity of Vero-R-1 cells decreased with increasing number of passages. Cells destroyed by freezing and drying or cell-free culture fluid did not induce tumors. Co-cultivation of Vero-R-1 cells with chick embryo fibroblasts for 5-26 days induced infectious RSV production as demonstrated by tumor production in chicks after inoculation of cell-free culture fluid. Vero-R-1 cells (10^{-5}) produced tumors in cheek pouches of golden hamsters (60 g), but no tumors occurred in cheek pouches inoc. with normal Vero cells.

70-276 GROWTH AND NUCLEIC ACID SYNTHESIS IN NORMAL CELLS AND CELLS INFECTED WITH ROUS SARCOMA VIRUS. (E.) Colby, C. (U. California San Diego, La Jolla) and H. Rubin. J. Nat. Cancer Inst. 43(2):437-444, 1969.

Normal chick embryo cells (CEC; $4 \times 10^6/50$ mm petri dish) and CEC infected with Rous associated virus (RAV; multiplicity of infection = 1.0) stopped growing within 24 hr. DNA and RNA synthesis decreased in both during the first 48 hr. However, CEC infected as above with Rous sarcoma virus (RSV) continued growing up to 48 hr., and DNA and RNA synthesis continued at constant rates. At 48 hr. RAV-infected cells were resistant to a dose of RSV which produced 1500 foci on normal cultures. The growth-inhibited state of normal cells could be released by changing the growth medium, thus obliterating the differences in nucleic acid synthesis and growth rate between normal and RSV-infected cells.

70-277 MALIGNANT AND TRANSFORMING ACTIVITY OF ROUS SARCOMA VIRUS. II. THE STUDY OF VARIANTS OF ROUS SARCOMA VIRUS ISOLATED FROM MOUSE TUMOURS. (E.) Obukh, I. B. (Gameleia Inst. Epidemiol. Microbiol., Moscow) and I. N. Kriukova. Int. J. Cancer 4(6):809-812, 1969.

Rous sarcoma virus (RSV) isolated from mouse tumors (originally induced by inj. of cell cultures infected with Carr-Zilber strain) by passage through chicks induced tumors in 60-88% of newborn, suckling, and adult Af mice. The highest incidence was seen in newborns; and the longest latent period (5 mo.) was seen in adults. Carr-Zilber virus did not induce tumors in any of the mice. The virus variants isolated from the mouse tumors were also highly oncogenic for adult and suckling golden hamsters (3 mo. and 10 days, resp.). Carr-Zilber virus induced tumors only in suckling hamsters. The coat antigens of the isolated viruses were not different from those of the original strain. An RSV variant was isolated from transformed nonmalignant cultures by means of fusion with normal chick embryo fibroblasts. This virus did not differ from variants isolated from mouse tumors in its oncogenicity for adult hamsters and mice.

70-278 MALIGNANT AND TRANSFORMING ACTIVITY OF ROUS SARCOMA VIRUS. I. MALIGNANT EFFECT OF ROUS SARCOMA VIRUS. (E.) Obukh, I. B. (Gameleia Inst. Epidemiol. Microbiol., Moscow), I. N. Kriukova, T. I. Biriulina and N. N. Kuznetsova. Int. J. Cancer 4(6):799-808, 1969.

Oncogenicity for syngeneic animals developed rapidly in cell cultures of embryos from C3H-H2 and (CBAT6T x Af)_{F1} mice after exposure to Rous sarcoma virus (RSV; Carr-Zilber strain). Admin. of 3×10^6 syngeneic cells harvested on day 10 after RSV infection resulted in tumor development in mice (strain above). Cells became highly oncogenic immediately after RSV exposure; the latent period for tumor development was 9.5 mo. However, if the cells were cultivated for several days after virus exposure, the latent period was reduced to < 4 mo. Cultures retained their oncogenicity for 14 days. (When the

infected cells became transformed in morphology, they lost their oncogenicity for syngeneic animals). The tumors induced in mice were virogenic and contained the group-specific antigen of avian sarcoma-leukosis complex.

70-279 SPECIFIC TRANSPLANTATION RESISTANCE AGAINST MOUSE TUMOUR INDUCED BY MOUSE SARCOMA VIRUS (HARVEY). (E.) Koldovsky, P. (Czechoslovak Acad. Sci. Inst. Exp. Biol. Genet., Prague), A. Turano and G. Fadda. Folia Biol. (Praha) 15(3):224-225, 1969.

Five groups of female C57BL/6 and BALB/c mice were immunized (s.c. inj.) with allogeneic tumor tissue (Swiss tumor induced by Mouse Sarcoma Virus; MSV), subminimal dose of syngeneic C57BL/6 *in vitro* transformed cells, BALB/c cells transformed *in vitro*, Moloney Leukemia Virus (MLV), or MSV and male organ tissues (controls). The animals were challenged 4 weeks after immunization with cell suspensions of syngeneic MSV (Harvey) induced tumor (MSVT). All controls (6/6) and 1/10 of the group immunized with a subminimal dose of C57BL/6 *in vitro* transformed cells developed tumors, all other animals were completely resistant. It is suggested that MLV and MSV contain the same genetic information for tumor-specific antigen and that MSV is possibly a mutant of MLV.

70-280 KARYOLOGICAL ANALYSIS OF MOUSE AND RAT EMBRYO CELLS TRANSFORMED BY MURINE SARCOMA VIRUS (HARVEY). (E.) Donner, L. (Czechoslovak Acad. Sci. Inst. Exp. Biol. Genet., Prague), A. Turano and J. Bubenik. Folia Biol. (Praha) 15(3):226-228, 1969.

Mouse sarcoma virus (Harvey) was added to 13-day-old mouse (C57BL/6) and 18-day-old rat (Wistar) embryo cells. Foci of morphologically transformed cells appeared 2-3 weeks later. After 3-5 weeks the cultures contained 80-90% altered cells. Inj. of culture fluid from these transformed cultures induced s.c. sarcomas in newborn mice and rats 2-3 weeks after inj. Karyological analysis of mouse cells 15 weeks after transformation revealed 2 modal classes: a large with 40 and a smaller with 80 chromosomes. All karyotypes were diploid, endoreduplication was seen in 5/100, single chromatid breaks or small acentric fragments in 4/50 metaphases. No increased incidence of secondary constrictions was observed. Karyological examination of rat cells 1 and 4 weeks after transformation revealed that they retained the normal diploid number of chromosomes and no aberrations were observed. It is concluded that no significant chromosomal changes are induced by MSV (Harvey).

70-281 STUDIES ON MURINE SARCOMA VIRUS: A MORPHOLOGICAL COMPARISON OF TUMOR-GENESIS BY THE HARVEY AND MOLONEY STRAINS IN

MICE, AND THE ESTABLISHMENT OF TUMOR CELL LINES. (E.) Berman, L. D. (Boston City Hosp., Mass.) and A. C. Allison. Int. J. Cancer 4(6):820-836, 1969.

Newborn and older CBA, IC and BALB/c mice were inoc. with Moloney or Harvey strain murine sarcoma virus (MSV-M, MSV-H; i.m.; i.p. or s.c.). Results with the two strains were somewhat similar but MSV-H seemed somewhat more potent, producing death in a larger percentage of animals. Erythroblastic splenomegaly was a distinctive feature of disease produced by MSV-H. Solid tumors induced by both viruses were similar in morphology, but some consistent differences were noted. The tumors appeared to arise by massive recruitment of primitive mesenchymal cells rather than by clonal proliferation.

70-282 INTRACYTOPLASMATIC GLYCOGEN DEPOSITS, LAMELLATE STRUCTURES AND VIRUS-LIKE INCLUSIONS IN MAST CELL TUMORS OF DOGS. AN ELECTRON-MICROSCOPIC STUDY. (Ger.) Rudolph, R. (Justus Liebig U., Giessen, Germany) and E. Weiss. Z. Krebsforsch. 72(4):343-349, 1969.

Electron microscopy of tumor tissue from a 2-yr.-old dog with mast cell sarcomatosis revealed 3 types of structures: 1) Intracytoplasmatic glycogen grains occurring either singly or in aggregates: the diameter of single grains was 100-300 Å while aggregates measured up to 6 µ. These glycogen deposits were never found in nuclei. 2) Round or oval "lamellar bodies" measuring up to 1.5 µ and consisting of either a few or several lamellae. 3) Intracytoplasmatic virus-like particles consisting of an inner core and outer shell. They occurred either singly or in small loose aggregates in the archiplasm or in dense groups surrounded by a single membrane in the cytoplasm. Including the shell they measured 26-36 µ.

70-283 SKELETAL AND RETICULAR TISSUE DISORDERS PRODUCED IN MICE BY AGENT(S) FROM SARCOMA 37. (E.) Merwin, R. M. (NCI, Bethesda, Md.) and L. W. Redmon. J. Nat. Cancer Inst. 43(2):365-376, 1969.

A filterable, serially transmissible agent which caused skeletal changes in BALB/c mice was isolated from Sarcoma 37 (transplanted for 238 generations in strain A/LN mice). Tumor tissue inoc. s.c. in the axillary region or macerated tissue placed i.p. in diffusion chambers produced intramembranous ossification in the distal large limb bones, moving to the proximal limb bones, sternum and other bones later. The isolate also caused reticular tissue disorders including splenomegaly, lymphocytic neoplasms, and type B reticulum cell neoplasms. Skeletal changes occurred most frequently in mice with reticular tissue disorders. Skeletal abnormalities were induced only in BALB/c and BALB/c

hybrid mice although the agent was transmitted by mice of other strains. Moloney leukemia virus also produced skeletal changes.

70-284 STUDIES ON GROUP-SPECIFIC ANTIGENS IN TUMOURS INDUCED WITH AVIAN TUMOUR VIRUSES IN RATS. (E.) Thurzo, V. (Slovak Acad. Sci. Cancer Res. Inst., Bratislava, Czechoslovakia), M. Šimkovičová and D. Šimkovič. Int. J. Cancer 4(6):852-858, 1969.

High titers of group specific complement-fixing antigen (GS) were seen in all primary tumors induced in 7-21-day-old White Leghorn chicks with Bratislava 77 virus (B77V) when studied with high-titer rabbit antiserum against a purified GS antigen of avian myeloblastosis virus. All B77V-induced tumors in white Peking ducks (1 day old) also had high titers. High GS antigen titers were detected with rabbit antiserum in 3/6 B77V-induced rat tumors (2/3 virus producing). GS antigen was not detected with rabbit antiserum in 3/6 rat tumors, but sera obtained from these rats contained high titers of GS antibodies when examined with different GS antigens. High GS antigen titer was also seen with Prague strain Rous Sarcoma virus-induced rat tumor. All attempts to detect GS antigen in one Schmidt-Ruppin strain Rous sarcoma virus-induced tumor were negative.

70-285 DEMONSTRATIONS OF TUMOR-SPECIFIC IMMUNITY AGAINST ANTIGENS UNRELATED TO THE MAMMARY TUMOR VIRUS IN SPONTANEOUS MAMMARY ADENOCARCINOMAS. (E.) Morton, D. L. (NCI, Bethesda, Md.), G. F. Miller and D. A. Wood. J. Nat. Cancer Inst. 42(2):289-301, 1969.

This study reports an attempt to induce immunity against 11 spontaneous mammary adenocarcinomas in C3H/HeN and DBA/2JN mice congenitally infected with mammary tumor virus (MTV). Five of the tumors were immunogenic to the inbred strain of tumor origin. Sensitization by either temporary tumor growth followed by excision or retreatment with irradiated tumor tissue was effective in eliciting immunity. The tumor-specific immunity induced by temporary tumor growth was individually specific against the neoplasm used for immunization, and no cross-immunity was seen. Use of the same tumor for both sensitization and challenge did not result in significant enhancement of tumor growth. Since both immunogenic and nonimmunogenic tumors arose from the same mouse, it was concluded that immunogenicity was not related to genetic origin of the neoplasm. There was some correlation between the type of neoplasm and immunogenicity; 11/3 type A tumors were immunogenic, while only 1/6 type B tumors were immunogenic. The immunogenicity was concluded to be tumor-specific, since normal tissues from the same mouse in which the tumor originated, or from isogenic mice, would not immunize against tumor challenge.

It was also concluded that the immunity was not related to MTV-infection.

70-286 RESPONSE OF HYPERPLASTIC ALVEOLAR NODULE OUTGROWTH-LINE D1 TO MAMMARY TUMOR VIRUS, NODULE-INDUCING VIRUS, AND PROLONGED HORMONAL STIMULATION ACTING SINGLY AND IN COMBINATION. (E.) Medina, D. (U. California Cancer Res. Genet. Lab., Berkeley) and K. B. DeOme. J. Nat. Cancer Inst. 42(2):303-310, 1969.

The nodule outgrowth-line D1 was derived from a nodule found in a 17-mo.-old BALB/cCrg1 female mouse, which had received daily s.c. inj. of 1 µg estradiol and simultaneously stimulated by 3 pituitary isografts at 2-5 mo. of age. Hosts received D1 nodule transplantation at 3 weeks of age; prolactin-secreting pituitaries were transplanted into host fat pads at 3-5 mo. Seventy nine percent of the D1 nodule outgrowths in BALB/c f. C3H mammary tumor virus (MTV)-positive female virgins produced tumors with a mean latent period of 284 days. Tumors arising from D1 nodule outgrowths of mice infected with nodule-inducing virus (NIV) appeared later in life and in lower frequency. The tumor incidence in D1 nodule outgrowths in MTV-negative, NIV-positive (C3Hf x BALB/c)F₁ hybrids was significantly greater than that in MTV-negative, NIV-negative BALB/c mice. Apparently, NIV is not as effective as MTV in inciting neoplastic transformation among D1 nodule cells. The data suggest that prolonged hormonal stimulation exerts only a synergistic effect on tumor production with either MTV or NIV. It is concluded that the tumor-producing capabilities of a nodule are determined by the type of virus it contains.

70-287 DEMONSTRATION OF NEW STAGES IN THE EVOLUTION OF MAMMARY TUMOR VIRUS IN THE MOUSE: INTRACYTOPLASMIC VIRAL INFRA-PARTICLES AND THE FORMATION OF PARTICLE A. (Fr.) Thomas, J. A. (Ctr. Cell Physiol., Paris), E. Hollande, M. Henry and M.-C. Dutrillaux-Ducros. C. R. Acad. Sci. [D] (Paris) 270(3):574-577, 1970.

Electron microscopy of 630 sections of spontaneous mammary tumor or tumor appearing after inoc. of Swiss mice with MTV virus disclosed the presence of intracytoplasmic infraparticles in 6 developmental stages, culminating in one which closely resembled viral particle A. Stage I consisted of a dense central nodule (approx. diameter, 140 Å) surrounded by a clear space delimited by a discontinuous, granular corona (approx. diameter, 580 Å). The adjoining hyaloplasm was disposed in what appeared to be numerous, arching bridges, the whole attaining a diameter of > 2300 Å. In Stage II, these "bridges" were reduced in number and size and assumed a more radial distribution, while the central nodule, appearing to be breaking up, was still attached

to the corona by a curving stream of granules. In Stage III, the central nodule (approx. diameter, 330 Å) was surrounded by a clear space, the delimiting corona was less discontinuous and more dense. In Stage IV, a clear central zone with some residual dark granules was surrounded by a continuous, irregular corona (approx. diameter, 610 Å) whose internal surface appeared to hold the material which had formed the central nodule of the previous stages. In Stage V, the clear zone and its corona were surrounded by 2 concentric, annular zones (dense and relatively clear, resp.). In Stage VI, these annular zones were clearly individualized. At this stage, as compared to viral particle A, the central zone is somewhat more dense, the corona somewhat less regular, and the overall size somewhat smaller.

70-288 ANTIGENIC DIFFERENCES AMONG VIRUS-INDUCED MOUSE MAMMARY TUMORS ARISING SPONTANEOUSLY IN THE SAME C3H/Crg1 HOST. (E.) Vaage, J. (U. California Cancer Res. Genetics Lab., Berkeley), T. Kalinovsky and R. Olson. Cancer Res. 29(7):1452-1456, 1969.

Spontaneous mammary carcinomas were removed from C3H/Crg1 (C3H) breeding female mice and implanted s.c. in the right flank of 12-16-week-old female C3H (infected with mammary tumor virus, MTV) and MTV-C3Hf/Crg1 (C3Hf) hosts. When tumors reached a size of 15 X 15 mm, they were removed and a suspension was prepared from a C3H tumor; 10⁵ living cells were then inj. into the left flank of pretreated and nontreated control C3H and C3Hf mice. Of 19 spontaneous mammary carcinomas from 4 C3H females, all were tested for antigenicity in C3H hosts and 17 were tested in C3Hf hosts. All of the latter were immunogenic in C3Hf hosts, while only 5/19 induced resistance to challenge in C3H hosts. The antigenicity seen in the MTV-free hosts is considered to be due to virus-associated transplantation antigens (VATA), while the results in the MTV-infected C3H hosts suggest that the 5 tumors involved possess tumor-specific non-VATA. In cross-reactivity studies, 3 mammary tumors from 3 different donors induced a nonspecific resistance to challenge in C3Hf hosts. Each tumor, when used to immunize, protected against challenge with all 3 tumors.

70-289 A NEW APPROACH TO MAMMARY TUMORIGENESIS IN RODENTS. (E.) DeOme, K. B. (U. California Cancer Res. Genet. Lab., Berkeley) and D. Medina. Cancer 24(6):1255-1262, 1969.

Hyperplastic alveolar nodule outgrowth lines which did not carry the mammary tumor virus or its variant and were not induced by chemical carcinogens or irradiation were maintained in intact BALB/c virgin female mice. Each of these hormone-induced outgrowth line has its characteristic tumor incidence. Mammary tumor virus, its variant, gamma irradiation, and 7

known carcinogens all increased the known tumor incidence of the nodules. The authors suggest the use of nodules in testing carcinogenicity.

70-290 ADENOCARCINOMAS AND LEUKEMIAS INDUCED BY THE MEDIA OF IN VITRO CULTURES OF MAMMARY TUMORS. (Fr.) Mouriquand, C. (Ctr. Nuclear Study Lab. Cell. Biol., Grenoble), J. Mouriquand and C. Viala. C. R. Acad. Sci. [D] (Paris) 270(2):444-447, 1970.

Three spontaneous mammary tumors derived from PS mice were cultured by conventional methods (no additional details). On day 3, 5 and 7, the cell-containing supernatant was withdrawn and centrifuged at 1000 g x 10 minutes, to eliminate the cells; then at 60,000 g x 60 minutes. The resulting residua and supernatants were inoc. separately into 3-week-old mice of the same strain (0.25 ml, single i.p. dose). Multiple mammary adenocarcinomas developed in 2-19 animals receiving the 3-, 5- or 7-day residua; leukemia, in 7-19; both, in 7-19; 3-19 failed to respond. (Mean latent periods were 8-10 mo., 46-57 days, and 54 days, resp.). Comparable tabulations for 31 animals receiving supernatants were 4, 17, 2, and 8, resp., with mean latency periods of 3-10 mo., 58-106 days, and 49 days, resp. Cells removed from the culture on day 5 and 7, prior to centrifugation, showed the presence of numerous, mature, Type C viral particles. In one of the 5-day samples only, a group of Type B viral particles was also found. No Type A particles were observed in any sample. In a correlative study, with centrifugation at 1000 g x 15 minutes and 105,000 g x 180 minutes, 2 multiple mammary adenocarcinomas and 1 metastasizing, malpighian carcinoma of the uterus developed in 6 animals inoc. with 3-, 5- or 7-day residua, all after latency periods of < 3 mo. Among an unspecified number inoc. with 5- or 7-d supernatants, 2 unspecified mammary tumors developed after 2.5 and 4.5 mo., resp. No leukemias developed in either group in this correlative study.

70-291 PRECANCEROUS AND CANCEROUS LESIONS OF THE MAMMARY GLAND IN MICE OF THE NZB STRAIN. (Fr.) Hollmann, K. H. (Broussais Hosp. Cytopath. Lab., Paris) and J. M. Verley. C. R. Acad. Sci. [D] (Paris) 270(2):448-450, 1970.

Histologic study of the mammary glands of NZB mice showed the presence of multiple, precancerous lesions in 9/10 multiparous animals aged > 8 mo. In 7/9, hyperplastic, alveolar lesions were seen, consisting of alveoli surrounded by actively secreting cells, such as those observed during pregnancy. The alveoli themselves were surrounded by fat and filled with secretory material. In 2/9, epidermoid lobuli surrounded by fibrous connective tissue were found, suggesting the initial stages of small, keratinizing cancers. When 4 females,

aged > 12 mo., received pituitary grafts, the incidence of hyperplastic alveolar lesions was increased significantly, and 3/4 developed small mammary carcinomas. This apparent, latent susceptibility of the strain contrasts with the relative infrequency of actual mammary cancer, a phenomenon which may be due either to the animal's peculiar immunologic status or to an inherent ability to modify viral particles.

- 70-292 HORMONAL CONTROL OF DNA SYNTHESIS: ALTERED RESPONSIVENESS OF HYPERPLASTIC ALVEOLAR NODULES OF MOUSE MAMMARY GLAND. (E.) Banerjee, M. R. (U. Nebraska Inst. Cell Res., Lincoln). J. Nat. Cancer Inst. 42(2):227-234, 1969.

Bilateral oophorectomy demonstrated that DNA synthesis in the normal mammary gland of virgin C3H and BALB/c mice is dependent on the presence of the ovaries. Mammary tumor virus (MTV)-induced C3H-hyperplastic alveolar nodule (HAN) outgrowths were able to synthesize new DNA in the absence of ovaries, suggesting that C3H-HAN tissues possess an altered responsiveness to ovarian hormonal control of DNA synthesis. DNA synthesis in BALB/c-HAN tissue was dependent on the presence of ovaries. With regard to the maintenance of characteristic lobuloalveolar differentiation, both C3H and BALB/c HAN were of similarly altered responsiveness. It is suggested that the hormones controlling DNA synthesis and the maintenance of lobuloalveolar structures in HAN tissue may function at different levels. The decreased DNA synthesis in BALB/c-HAN may reflect some change in the sequence of hormonally controlled metabolic events culminating in a failure to initiate DNA synthesis.

- 70-293 STUDIES OF HUMAN MILK IN RELATION TO THE POSSIBLE VIRAL ETIOLOGY OF BREAST CANCER. (E.) Feller, W. F. (5255 Loughboro Rd., N. W., Washington, D. C.) and H. C. Chopra. Cancer 24(6):1250-1254, 1969.

Electron microscopic examination of purified milk pellets from 8/12 women with confirmed breast cancer showed the presence of distinct, small virus-like particles in the milk. The particles were 20-40 μ ; with an electron dense nucleoid surrounded by a double limiting membrane. The particles occurred in clusters. A second type of particle, a larger oncornavirus-type was seen in milk specimens from 5 of 12 breast cancer pts. The overall diameter was 100-140 μ and the particles exhibited many morphological characteristics of known murine oncogenic RNA viruses. Specimens from the milk of normal women also contained the two virus-like particles: 7/43 exhibited the small particles but only 1/43 revealed the presence of the larger particle; this woman had a positive family history of breast cancer.

- 70-294 VIRUSES AS POSSIBLE ETIOLOGIC FACTORS IN HUMAN BREAST CANCER. (E.)

Dmochowski, L. (U. Texas M. D. Anderson Hosp., Houston), G. Seman and H. S. Gallager. Cancer 24(6):1241-1249, 1969.

At electron microscopy 14/44 breast cancer biopsy specimens were found to contain structures resembling virus particles: 8/14 type B; 4/14 type C and 13/14 small virus-like particles (SVP). No correlation was seen between different types of virus-like particles and age of pt., or type of tumor. Virus-like particles resembling type B, type C and SVP also were seen in 1/2 fibroadenoma pts. After serial passage in vitro, SVP were seen in the 3 tumors (2 nodular; 1 stellate) studied to date.

- 70-295 INTRANUCLEAR VIRUS-LIKE PARTICLES IN A MAMMARY CARCINOMA. (Ger.) Schäfer, A. (U. Mainz Path. Inst., Germany). Experientia 25(7):729-732, 1969.

Electron microscopic examination of material from a predominantly solid, mostly scirrhous carcinoma removed from a 54-yr.-old pt. revealed 3 kinds of nuclear inclusions: 1) chiefly hexagonal (indicating an icosahedral structure) electron dense particles with a diameter of 54-80 μ and surrounded by a halo of weakly electron dense substance. The internal structure of these particles was not homogeneously osmophilic but was composed of smaller subunits of 40-45 \AA diameter. 2) Clusters of smaller (200-300 \AA) and larger (300-400 \AA) granula which were frequently surrounded by the larger particles. In these granula a cross-striated pattern of 40-45 \AA wide subunits was discernible. 3) Bundles of 170 \AA wide filaments on the periphery and in close association with the granules and also composed of 40-45 \AA subunits in cross-striation pattern. It is suggested that these nuclear inclusions constitute virus particles, viruses at an early stage of development and C) virus protein subunits.

- 70-296 BIOLOGY OF HERPES-TYPE VIRUS ASSOCIATED WITH BURKITT LYMPHOMA CELL LINES.

(E.) Hinuma, Y. (Tohoku U. Sch. Dent., Sendai, Japan). Gann Monogr. 7:65-76, 1969.

Previously reported data on EB virus isolation, in vitro replication and immunodiffusion and fluorescence detection are reviewed. The incidence of EB antibody in sera of normal individuals in the Akita prefecture in northern Japan is 80% among infants up to 3 yr. old and 80-100% in adolescents and young adults (up to 40 yr.). It is suggested that the EB virus has a cell transforming potential and that people with EB antibodies have virus infected ("transformed") cells. These are held in check and do not grow in vivo due to an as yet unknown in vivo

repression mechanism. In a "de-repressed" state these cells can grow rapidly developing into a tumor (Burkitt lymphoma in the tropics). The mode of EB virus transmission, horizontal versus vertical is discussed and it is suggested that the great incidence among infants in Japan could indicate possible vertical transmission.

- 70-297 HERPES-TYPE VIRUS INFECTION IN HUMAN EMBRYO CELLS IN VITRO: ENTRY, REPLICATION, AND CHROMOSOMAL ABERRATIONS. (E.) Osato, T. (Hokkaido U. Sch. Med., Sapporo, Japan), K. Yamamoto and K. Sugawara. Gann Monogr. 7: 173-182, 1969.

Human embryo lung cells exposed for 60 min. at 36 degrees to herpes-type virus (HV), from human THE-3 cells showed virus particles within the cytoplasm or near the cell surface. After mixed cultivation of lung cells (2×10^6) and THE-3 cells (2×10^7), specific immunofluorescence appeared in a number of embryonic lung cells after 5 days and increased with continued incubation. A relatively high incidence of chromatid and chromosome breaks was seen in embryonic lung cells exposed to the extract from HV-containing THE-3 cells.

- 70-298 TRANSFORMATION IN VITRO OF HUMAN EMBRYO TISSUES BY HUMAN LEUKEMIC CULTURE FLUID. (E.) Osato, T. (Hokkaido U. Sch. Med., Sapporo, Japan) and Y. Ito. Gann Monogr. 7:95-103, 1969.

Proliferative transformed foci composed of round or epitheloid cells were obtained in 37/126 human embryo cultures 23-76 days after exposure to cell-free human leukemic culture fluid (from 6/14 patients with acute or chronic myelogenous leukemia). Several factors which influenced transformation efficiency are presented. Immunofluorescence studies showed that the transforming capacity of leukemic cultures correlated with the number of fluorescing leukemic cells obtained after exposure to serum containing antibodies against herpes-type virus. Three transformed cell lines, THE-1, THE-2, and THE-3 were established and a herpes type virus was demonstrated by electron microscopy and immunofluorescence in some cells of these transformed cell lines. The possibility of a viral agent as the cause of the transformation and of human leukemia is discussed.

- 70-299 CONTINUOUS SUSPENSION CULTURE OF HUMAN NEOPLASTIC LYMPH NODES: CELL IDENTIFICATION AND DETECTION OF HERPES-TYPE EB VIRUS. (E.) Oboshi, S. (Nat. Cancer Ctr. Res. Inst., Tokyo). Gann Monogr. 7:191-203, 1969.

Continuous cell lines were established from human lymph node biopsies from pts. with infiltration of acute myeloid leukemia (RS-2), curing

process of Hodgkin's disease by chemotherapy (RS-3), and metastases from stomach cancer (MC-8; MC-12). EB virus antibodies in low titers were found in all sera. The cells grew singly and in aggregates unattached to the surface of the petri dishes. Cell doubling time ranged from 24-36 hr. The RS-2 and RS-3 lines were composed of lympho-reticular cells; the MC-8 and MC-12 were mixed cancer cells and lympho-reticular cells. All cultures contained cells capable of synthesizing immunoglobulins. EB virus particles were detected only in the nuclear debris of a degenerating cell of the RS-2 line.

- 70-300 DIRECT MEMBRANE FLUORESCENCE REACTION OF EBV-CARRYING HUMAN LYMPHOBLASTOID CELLS: BLOCKING TESTS WITH XENOGENEIC ANTISERA. (E.) Bremberg, S. (Karolinska Inst. Sch. Med., Stockholm), G. Klein and A. Epstein. Int. J. Cancer 4(6):761-766, 1969.

In direct membrane fluorescence reaction between a fluorescein-conjugated antiserum of a Burkitt lymphoma patient and the herpes type EB virus (EBV)-carrying human lymphoblastoid cells, the serum of a rabbit immunized with EB virus concentrate produced a fair to very good blocking of the reaction. The sera of rabbits immunized with chronic lymphatic leukemia cells were free from significant blocking activity. Sera of rabbits immunized with Burkitt lymphoma biopsies produced significant blocking. The authors concluded that the EBV-determined antigen receptors could be distinguished from species-specific membrane antigen sites.

- 70-301 SOME FACTORS AFFECTING MEMBRANE IMMUNOFLUORESCENCE REACTIVITY OF BURKITT LYMPHOMA TISSUE CULTURE CELL LINES. (E.) Yata, J. (U. Tokyo) and G. Klein. Int. J. Cancer 4(6):767-775, 1969.

Two established cell lines of Burkitt's lymphoma were tested to determine optimum culture conditions for membrane immunofluorescence (MIF). Although the two lines behaved somewhat differently, they both had better reactivity when maintained at a high concentration, as long as crowding did not prevent multiplication. More closely packed cells within a smaller bottom area of the culture vessel exhibited better MIF reactivity than more dispersed cells (conditions of medium supply and depth of fluid phase were identical for the two lines). Under different conditions of growth, an inverse relationship between rate of cell multiplication and the percentage of viable MIF-positive cells was seen.

- 70-302 MEMBRANE IMMUNOFLUORESCENCE REACTIONS OF "TRANSFORMED" HUMAN CELL LINE THE-3. (E.) Yoshida, T. O. (Aichi Cancer Ctr. Res. Inst., Nagoya, Japan) and Y. Ito. Gann Monogr. 7:205-209, 1969.

In immunofluorescence studies the THE-3 cell line (human embryonic cells "transformed" after exposure to human leukemic cell culture fluid) could react with membrane immunofluorescence-positive sera from Burkitt lymphoma patients, but the pattern was not highly significant. The fluorescence index, however, indicated differences between Burkitt lymphoma cell lines and control human embryonic cells. Negative control sera did not react significantly with Burkitt lymphoma cell lines, "transformed" THE-3 cell line, or with human embryonic cells.

- 70-303 REPRESSION OF BENZO[a]PYRENE TUMORIGENESIS BY AGENTS PRESENT IN CELLS INFECTED OR TRANSFORMED BY TYPE 12 ADENOVIRUS. (E.) Pinkerton, H. (St. Louis U. Sch. Med., Mo.), P. I. S. Liu and E. S. Goodman. Proc. Soc. Exp. Biol. Med. 131(2):621-625, 1969.

Benzo(a)pyrene(BP)-induced tumor growth was significantly retarded in male and female Syrian hamsters admin. unpurified, active or heat-inactivated adenovirus 12 (Ad12; 0.1 ml; s.c.) or sonicated virus-free Ad12-transformed hamster embryo cells (HET; 4-7 x 10⁷ cells; s.c.) before an initial BP (3 mg; s.c.) inj. and 60 and 100 days after BP. Maternal immunization with Ad12 or HET similarly retarded the development of BP-induced tumors in offspring, when the initial BP inj. was admin. at 3 weeks of age. BP-induced tumors first appeared 115-140 days after the first BP inj., and the number of inj. and/or their spacing had no effect on the induction period or growth rate.

- 70-304 ANTIBODY TO ONCOGENIC VIRUSES IN SERA OF CANCER PATIENTS. (E.) Ishii, K. (Nat. Cancer Ctr. Res. Inst., Tokyo), K. Koyama, H. Shimojo, A. Kawamura, Jr., Y. Aoyama and K. Nishioka. Gann Monogr. 7:157-162, 1969.

Examination of sera from cancer pts., non-cancer pts. and normal subjects by the complement fixation and indirect immunofluorescent tests revealed antibodies to the adenovirus Type 12 (AV-12) T (tumor) antigen in a larger percentage of cancer pts. (8.5%) than in non-cancer pts. (3%) or healthy controls (0.8%); antibodies to AV-12 V (viral) antigen were found in 20.4%, 6% and 5.3%, resp. Positive complement fixation reactions were obtained in only a small percentage of sera with Rous sarcoma virus (RSV)-gs (group-specific) antigen (3.7%, 6.0% and 1.1%, resp.) and SV40 V antigen (0.6%, 3.0%, resp., normal not determined) but none were positive with SV40 T antigen. The number of positive reactions was highest with AV-12 T antigen in cancer of the esophagus (10%), lungs (6.6%), stomach (6.3%) breast (3.5%), cervix (3.2%), and with AV-12 V antigen in cancer of lungs (26.0%), cervix (25.8%), breast (21.4%), esophagus (15.0%) and stomach (10.3%).

- 70-305 ONCOGENIC SIMIAN ADENOVIRUSES. V. RECOVERY OF INFECTIOUS VIRUS FROM INTRACRANIAL TUMOR CELLS INDUCED BY SIMIAN ADENOVIRUS 7. (E.) Slifkin, M. (U. Pittsburgh Sch. Med., Pa.), L. P. Merkow, M. Pardo and N. P. Rapoza. J. Nat. Cancer Inst. 43(2):423-435, 1969.

Simian adenovirus (SA7) inoc. into the right cerebral hemisphere of noninbred Syrian hamsters < 24 hr. old, induced intracranial neoplasms, which yielded infectious and oncogenic virus. The biological, biophysical, and morphological characteristics of this virus were consistent with SA7 and the virus was indistinguishable from SA7 by neutralization test. In s.c. neoplastic cells induced by the viral isolate and in LLC-MK₂ cells infected with the isolate the SA7 T antigen was found. Neoplastic cells induced by the isolate contained annulate lamellae.

- 70-306 SYNTHESIS OF ADENOVIRUS TYPES 5 AND 7 IN HeLa CELL CULTURES. (Rum.) Duca, M. (Inst. Med. Pharm., Iasi, Rumania), M. Alexandrescu, L. Handrache, L. Ionescu and E. Carasievici. Stud. Cercet. Infimicrobiol. 19(6):419-424, 1968.

Replication of adenovirus Type 5 (Prague strain) and adenovirus Type 7 (Iasi strain) in HeLa cells was studied. In cells infected with adenovirus Type 7 (1000 TCID₅₀), a quantitative relationship between the synthesis of infectious virus and hemagglutinating activity was found.

- 70-307 ELECTRON MICROSCOPE OBSERVATIONS ON VIRUS PARTICLES ASSOCIATED WITH A TRANSPLANTABLE RENAL ADENOCARCINOMA IN BALB/cf/Cd MICE. (E.) Felluga, B. (Int'l. Lab. Genet. Biophys., Naples, Italy), A. Claude and R. Mrena. J. Nat. Cancer Inst. 43(2):319-333, 1969.

A mouse substrain, BALB/cf/Cd, was developed by inbreeding and selection, with a renal tumor incidence of 60-70%. The spontaneous tumors were transplantable and no essential changes were observed in the growth characteristics or the microscopic appearance of the tumors, nor in the apparent cell-virus relationship in 200 consecutive grafting generations over a 5-yr. period. Virus particles were constantly observed in the cytoplasm of the tumor cells. The virus particles resembled virus particles seen in mouse mammary tumors and lymphomas in their morphology, morphogenesis, and distribution. They were carried over in cells through the process of mitosis.

- 70-308 CELLULAR IMMUNITY AND ITS SERUM-MEDIATED INHIBITION IN SHOPE-VIRUS-INDUCED RABBIT PAPILLOMAS. (E.) Hellström, I.

(U. Washington Med. Sch., Seattle), C. A. Evans and K. E. Hellström. Int. J. Cancer 4(5): 601-607, 1969.

San Juan and chinchilla rabbits of both sexes were inoc. with Shope papilloma virus (SPV) by scarification of the shoulder; regional axillary lymph nodes were subsequently removed as a source of lymph node cells (LNC). LNC from rabbits with persistent or spontaneously-regressed Shope papillomas were shown to equally inhibit colony formation of Shope papilloma and carcinoma cells; LNC from untreated rabbits or from rabbits with Shope virus-induced carcinomas failed to do this. Sera from rabbits with persistent Shope papilloma or carcinoma protected Shope tumor cells from regressor-LNC-induced inhibition; this was not seen with Shope papilloma regressor or untreated-rabbit sera.

70-309 PRECIPITIN RESPONSE OF CATTLE TO BOVINE PAPILLOMA VIRUS. (E.) Lee, K. P. (U. Wisconsin, Madison) and C. Olson. Cancer Res. 29(7):1393-1397, 1969.

Sera were obtained at successive intervals after exposure of 21 calves to bovine papilloma virus (BPV; initial i.v. inj. of BPV suspension followed by at least 9 successive exposures to BPV on the skin at intervals for 26 weeks. Precipitin-containing serum fractions were characterized by Sephadex G-200 gel filtration, DEAE cellulose chromatography, sucrose density gradient and analytic ultracentrifugation. Precipitins were found in 7/21 at 1 week, in 19/21 at 2, and in all by 8 weeks after exposure to BPV. The 2-mercaptoethanol (2-ME)-sensitive antibody was found in 7 at 1 week, 9 at 2 weeks, in only 2 at 4 weeks, and in none by 16 weeks. The 2-ME-resistant antibody appeared after 2 weeks and was present in all calves by 16 weeks. The 7S antibody precipitin was not affected by 2-ME, while 2-ME inactivated the precipitin activity present in the 19 S fraction. The 19 S antibody alone was present at 1-8 weeks, but could not be detected by 16 weeks. Both 7 and 19 S antibodies were found at 2-8 weeks. By 16 weeks, 7S antibody alone was detectable and only this antibody was seen in 3 calves at 4 weeks and in all at 16 weeks. Resistance to BPV reinfection followed the appearance of precipitins. The presence of serum precipitins bore no relation to the growth or regression of the papillomas.

70-310 THE ULTRASTRUCTURE OF CANINE CUTANEOUS PAPILLOMA. (E.) Watrach, A. M. (U. Illinois Coll. Vet. Med., Urbana). Cancer Res. 29(11):2079-2084, 1969.

Electron microscopic study of cutaneous papilloma biopsy material from 2 dogs revealed marked changes in the inclusion bodies of nuclei of epidermal cells. They consisted of aggregates of virus particles most frequently in the form

of closely packed crystalline arrays or, sometimes, as loose accumulations of particles randomly dispersed in the nuclear matrix. The particles of the closely packed formations were hexagonal in shape, ranging 450-490 Å in diameter. They consisted of a dense core 380-400 Å in diameter and an outer shell of approx. 40 Å thick. The center-to-center spacing was estimated at 530 Å. In some of the aggregates approx. 10% of the particles were devoid of the inner core. The particles in loose accumulations were approx. of the same size but tended to have a rounded shape. The described particles were morphologically identical to known papilloma viruses and are the first morphological indication of a viral agent in canine cutaneous papilloma.

70-311 STANDARDIZATION OF POLYOMA VIRUS INDUCED RAT TUMORS. (Ger.) Fasske, E. (Borstel Res. Inst., Hamburg, Germany), R. Fetting, J. Pokorný and H. Themann. Z. Krebsforsch. 73(2):122-135, 1969.

For experimental studies on DNA and RNA in tumors, it is very important to have standardized model tumors of isologous origin and of genetically identical hosts which develop at a constant rate and maintain a constant histomorphology. Inoc. (s.c.) of 0.2 ml (10^5 TCID₅₀) of Graffi polyoma virus BB/T2 (cultivated for 6 yr. in embryonic mouse cell culture) into newborn inbred Wistar rats induced various sarcomas and carcinomas after 6-10 mo. Five of these: a liposarcoma, a rhabdomyosarcoma, a fibrosarcoma, an alveolar adenocarcinoma of the salivary gland and a solid carcinoma, filled these requirements (rapid and constant rate of growth on subcutaneous transplantation, constant histomorphology) and were maintained by a constant transplantation method over a period of years in Wistar rats. The growth characteristics and histology of each type are described in detail. At the same time cell culture lines from these 5 tumors were maintained. When inoc. s.c. (5×10^5 cells in 0.1 ml) into 24-72 hr. old Wistar rats they developed into solid tumors.

70-312 THE FORMATION OF VARIANTS WITH A REVERSION OF PROPERTIES OF TRANSFORMED CELLS. III. REVERSION OF THE STRUCTURE OF THE CELL SURFACE MEMBRANE. (E.) Inbar, M. (Weizmann Inst. Sci., Rehovoth, Israel), Z. Rabinowitz and L. Sachs. Int. J. Cancer 4(5): 690-696, 1969.

The formation of variants from polyoma virus (PV)-transformed hamster embryo cells with a reversion of in vitro properties of transformation is associated with a partial or complete loss of agglutinability by the carbohydrate-binding protein concanavalin A (Con A). Treatment of variants with trypsin resulted in restoration of previously-lost agglutinability. Since the formation of variants was not associated with a

loss of ability to synthesize the virus-specific nuclear tumor (T) antigen, it is suggested that the synthesis of T antigen is insufficient to prevent reversion of cell surface architecture. Compared with parental transformed cells, variants with a partial or complete loss of agglutinability showed the same decrease in cloning efficiency in fluid medium and soft agar and in saturation density. Apparently both complete and partial reversion of Con A sites to the cryptic form can account for the same degree of reversion of in vitro properties. It is concluded that there is some minimal number of exposed sites for Con A which must be exceeded for the cells to express the properties of transformation in vitro.

70-313 NEW ANTIGENS IN CELLS TRANSFORMED BY THE SV40 VIRUS. II. EVIDENCE OF THEIR CYTOPLASMIC LOCALIZATION IN A CELL LINE (TSV5CL₂) OF HAMSTER FIBROBLASTS TRANSFORMED BY SV40. (E.) Tilz, G. P. (Univ. Clin., Graz, Austria), C. de Vaux Saint Cyr and P. Grabar. Int. J. Cancer 4(5):641-647, 1969.

Studies are presented which characterize the antibodies induced in Syrian hamsters by a clone of SV-40-transformed fibroblasts (TSV5CL₂). Immunochemical and immunocytological studies showed new antigens, not present in untransformed fibroblasts, localized in the cell cytoplasm, and inducing precipitating antibodies. Localization of the antigens was greatest in the microsomal-ribosomal fraction, less so on the cell membrane and not observed within the nucleus. The new antigens differed from the T antigen and from the transplantation antigen which is thought to localize on the cell surface. The anti-T antigen antibodies could be absorbed with a partially purified T antigen preparation, while the agglutinating antibodies were absorbable with membranes from TSV5CL₂ cells. Electron microscopy showed the presence of a latent hamster virus in both SV-40-transformed and in EHB control cells; the new antigens were not due to the presence of this virus.

70-314 THE LIPIDS OF NORMAL DIPLOID (WI-38) AND SV40-TRANSFORMED HUMAN CELLS. (E.) Howard, B. V. (U. North Carolina Sch. Med., Chapel Hill) and D. Kritchevsky. Int. J. Cancer 4(4):393-402, 1969.

Lipids were found to comprise 21% of the dry wt. of WI-38 cells; of this, 71% was phospholipid and 29% neutral lipid. SV-40-transformed WI-38VA13A cells had a lipid content of 18% of dry wt., with 59% phospholipid and 41% neutral lipid. The decrease in amount of phospholipid in transformed cells was significant, the difference in neutral lipid was not. In both cells, cholesterol and triglycerides were the main neutral lipids, with small amounts of cholesterol ester and mono- and diglycerides. In WI-38 and WI-38VA13A cells resp., lecithin

(57 and 57%) was the major phospholipid, but there were also appreciable amounts of sphingomyelin (7 and 13%), phosphatidyl ethanolamine (12 and 13%), phosphatidyl inositol (13 and 10%) and phosphatidyl serine (12 and 4%). Both cells showed appreciable amounts of free fatty acids. The major fatty acids in neutral lipids of WI-38 were palmitoleic and oleic, with appreciable quantities of stearic, linoleic, and arachidonic acids. Transformed cells showed a significant decrease in the amount of arachidonic acid and a significant increase in that of oleic acid. The fatty acid spectrum of WI-38 phospholipids was similar to that of neutral lipids, and there was a similar decrease of arachidonic acid in transformed cells. Both WI-38 and WI-38VA13A cells were able to incorporate ¹⁴C-acetate into neutral lipids and phospholipids, but these rates were not sufficient for cell growth, although the transformed cells showed an increase in cholesterol synthesis.

70-315 TRANSPLANTABLE MOUSE TUMOR LINE INDUCED BY INJECTION OF SV40-TRANSFORMED MOUSE KIDNEY CELLS. (E.) Kit, S. (Baylor Coll. Med., Houston, Tex.), T. Kurimura and D. R. Dubbs. Int. J. Cancer 4(4):384-392, 1969.

Cells from mKS-A cell lines (obtained by transformation of primary BALB/c kidney cultures with SV-40 clone 307L) were able to induce tumors in BALB/c and Swiss mice at passage 71 but not at passage 26. Tumors appeared after 7 days and beginning 51 days after inoc., could be serially transplanted, 14 times at 1-mo. intervals. At each of these passages, the SV-40 tumor (T)-antigen was present, suggesting that at least part of the SV-40 genome persisted. Sera from tumor-bearing mice fixed complement in the presence of SV-40 T-antigen. Five in vitro cell lines were established from tumors of different passages. Although infectious SV-40 was not extractable from any of these cells, it was recovered after heterokaryon formation with CV-1 cells. Serial transplantation was possible with cell lines derived from passages 8, 10 and 12, but not from passages 1 and 2. A 100% incidence of tumor production was seen with inoc. of 2 X 10⁴ cells from passage 8 or 10. Mice pre-immunized with SV-40-transformed cells (mKS-U13 and mKS-U17) failed to produce tumors after challenge with cell lines from passages 8 or 10, while nonimmunized control mice developed tumors after similar challenge. These results demonstrate that the passage 8 and 10 cells possess the SV-40 transplantation antigen and that these cells share a common antigen with mKS-U13 and mKS-U17 cells.

70-316 SIMIAN VIRUS 40 IN POLIO VACCINE: FOLLOW-UP OF NEWBORN RECIPIENTS. (E.) Fraumeni, J. F., Jr. (NCI, Bethesda, Md.), C. R. Stark, E. Gold and M. L. Lepow. Science 167(3914):59-60, 1970.

No cancer deaths were seen 8-yr. after a group of newborn children were admin. oral polio vaccine containing high titers of simian virus 40. Follow-up is being continued.

- 70-317 RELATION OF VIRUS-INDUCED CELL FUSION AND CHROMOSOME PULVERIZATION TO MITOTIC EVENTS. (E.) Takagi, N. (Roswell Park Mem. Inst., Buffalo, N. Y.), T. Aya, H. Kato and A. A. Sandberg. J. Nat. Cancer Inst. 43(2): 335-347, 1969.

In Chinese hamster embryo cells infected with Sendai virus, cell fusion occurred immediately after virus infection, and leveled off after 25 min. Chromosome pulverization was first seen 10 min. after virus infection and the incidence rose until 45 min.; but it suddenly fell to 25% of the max. value by 60 min. Pulverization usually occurred in multinucleate cells with at least one intact mitotic nucleus. The nucleus appeared susceptible to pulverization-inducing factors during S, G1, or G2 phases.

- 70-318 POLYNUCLEOTIDE LIGASE ACTIVITY IN CELLS INFECTED WITH SIMIAN VIRUS 40, POLYOMA VIRUS, OR VACCINIA VIRUS. (E.) Sambrook, J. (Cold Spring Harbor Lab. Quantitative Biol., Cold Spring Harbor, N. Y.) and A. J. Shatkin. J. Virol. 4(5):719-726, 1969.

- 70-319 DETECTION OF AGGLUTININS IN CHICKENS INFECTED WITH JM LEUKOSIS VIRUS. (E.) Zacharia, T. P. (U. Massachusetts Paige Lab., Amherst) and M. Sevoian. Appl. Microbiol. 19(1): 71-72, 1970.

- 70-320 KARYOTYPE STUDIES ON HUMAN LEUKEMIC LYMPHOBLASTS IN VITRO AND AS SERIAL TRANSPLANTS IN NEONATAL SYRIAN HAMSTERS. (E.) Krishan, A. (Harvard Med. Sch. Children's Cancer Res. Found., Boston, Mass.), R. Raychaudhuri and A. Flowers. J. Nat. Cancer Inst. 43(6):1203-1214, 1969.

- 70-321 MULTIPLICATION AND CYTOPATHOLOGY OF A PLANT TUMOR VIRUS IN INSECTS. (E.) Maramorosch, K. (Boyce Thompson Inst. Plant Res., Yonkers, N. Y.), E. Shikata, H. Hirumi and R. R. Granados. Nat. Cancer Inst. Monogr. 31:493-507, 1969.

- 70-322 PROPAGATION OF MAMMALIAN VIRUSES IN PROTISTA. IV. EXPERIMENTAL INFECTIONS OF *C. albicans* AND *S. Cerevisiae* WITH POLYOMA VIRUS. (E.) Kovács, E. (U. Toronto, Canada), B. Bucz and G. Kolompár. Proc. Soc. Exp. Biol. Med. 132(3):971-977, 1969.

- 70-323 VIRUS ASSOCIATED WITH EPIDERMAL HYPERPLASIA IN FISH. (E.) Walker, R. (Rensselaer Polytech. Inst., Troy, N. Y.). Nat. Cancer Inst. Monogr. 31:195-207, 1969.

- 70-324 EPIDERMAL HYPERPLASIA IN FISH: TWO TYPES WITH VISIBLE VIRUS. (E.) Walker, R. (Rensselaer Polytech. Inst., Troy, N. Y.). Nat. Cancer Inst. Monogr. 31:209-213, 1969.

See also abstract no.: 349

70-325 EPIDEMIOLOGY OF MALIGNANT TUMORS OF
THE RESPIRATORY TRACT. (It.) Grosso,
E. (U. Bari Inst. Hyg., Italy). Riv. Ist. Vac.
Consor. Prov. Antituber. 19(3):405-421, 1969.

In a study of lung cancer mortalities in Italy, mortality rates are expressed in terms of 100,000 population. Following a slow increase between 1932-1944 (from 2.3-4.1), the overall rate increased rapidly, to reach 21.7 in 1963. The greatest increase was for men (from 3.3 in 1932 to 36.8 in 1963, as compared to 1.3 and 7.1, resp., for women). The rate showed an abrupt upswing for men between 40-50 yr. of age (1963 = 25.0) and for women between 50-60 yr. of age (1963 = 12.2), peaking and then slowly leveling off thereafter (1963 = 201.5 for men aged 60-70 yr.; 41.7 for women aged 70-80 yr.). In a comparison of 14 countries, the Italian rate in 1959 was exceeded only by the United Kingdom, West Germany, and the United States, in descending order. The rate was lowest in Egypt and Colombia. A comparison of the mortality curve for 1932-1963 with one showing the consumption of tobacco in Italy confirms a significant correlation, as does a comparison of the mortality curve for 1950-1963 with one showing the consumption of petroleum products. A comparison of mortality data for 1961 in agricultural versus industrial areas of Italy also appears to show a significant correlation between lung cancer deaths and atmospheric and other environmental pollution, although these data may also be influenced by the percentages of the population belonging to different age groups.

70-326 RESULTS OF A STUDY OF THE STATE OF
HEALTH OF A POPULATION WITH A HIGH
INCIDENCE OF TUMOR MORTALITIES. (It.) Gallina,
F. (Civil Hosp., Spoleto, Italy), G. Chirico and
F. M. Zuccari. Ann. Sanit. Pubblica 30(2):215-
223, 1969.

A group of 1000 asymptomatic volunteers aged 40 yr. and over, drawn from an isolated mountain district and the immediately surrounding area in the district of Spoleto, Italy, underwent chest and g.i. X-ray screening, supplemented by blood tests and thorough personal histories, as part of an inquiry into the possible reasons for the high cancer mortality rate in the area (approx. triple the national av.). Among the disorders demonstrated were lung tumors in 2 men (1 advanced stage; 1 incipient), 2 cancers of the stomach (1 in a woman cholecystectomized 2 yr. previously; the other in a woman with a long-standing history of ulcer symptoms), 9 cases of gastric ulcer, 2 of Ménétrier's gastric adenomatosis, 1 of gastric polyposis, and 174 with increased erythrocyte sedimentation rate. It is suggested that the increased cancer death rate in this area may be due to an unusually high percentage of older people in the population (following

the "flight" of young people from this impoverished mountain area) and the custom of frequent inter-marriage of close relatives among the isolated group which has remained.

70-327 LUNG TUMORS IN THE PUBLIC HEALTH
HOSPITAL RECORDS OF THE PROVINCE OF
TREVISO DURING THE YEARS 1961 THROUGH 1965.
(It.) Mazzola, S. (Prov. Antitub. Soc., Treviso,
Italy) and A. Gerardi. Riv. Ist. Vac. Con. Pro.
Antitub. 17(1):75-78, 1967.

Records of the central public health hospital and 6 regional dispensaries in the province of Treviso, Italy showed that 162 pulmonary tumors were diagnosed during the yr. 1961-1965, inclusive, consisting of 8 benign tumors, 118 primary malignancies and 36 secondary malignancies, with a total occurrence of 5.3 tumors/10,000 pts. examined. Histological study of 8 primary tumors showed that 3/8 were adenomas, 3/8 were cystic teratomas, 1/8 (each) was a chondroma and a neurinoma. Among 24/36 secondary tumors which were identified, 12/24 were metastases of mammary carcinomas; 4/24, of unspecified uterine cancers; 3/24; of hypernephromas; 2/24 (each), of seminomas and unspecified cancers of the tongue; 1/24, of a malignant primary of unknown origin. Only 2/118 pts. were under 30 yr. of age; 5/118 were between 30-45 yr. of age; 111/118 were aged 46 yr. or older. The frequency of occurrence of primary pulmonary tumors (benign and malignant) increased progressively from 1.7/10,000 pts. examined in 1961 to 5.5/10,000 pts. examined in 1965.

70-328 CANCER MORTALITIES IN FRANCE IN 1967.
(Fr.) Brunet, M., J. Berlie and L.
Maujol. Bull. Inst. Nat. Sante 24(1):69-89,
1969.

A statistical study of cancer deaths in France during 1967 is presented, with breakdowns in terms of age groups, cancer sites, sex distribution by cancer sites, and distribution by geographic and political subdivisions. Also presented are estimates of the probable total number of cancer deaths when appropriate proportions of all deaths listed as due to unknown or poorly defined causes are added to the official registry. In general, the absolute number of cancer deaths had risen slightly, as compared to 1960, but the actual rate was not changed significantly. The over-all rate/100,000 in 1967 was higher in men than for women (234 and 182, resp.), with a combined rate of 208. The high rate by cancer site in men, was for bronchogenic and lung cancers (37.4/100,000); among women, it was for breast cancers (28.0/100,000). Mortality figures in the departments of France remained essentially stable as compared to those for preceding years.

70-329 CANCER MORBIDITY IN CARTAGENA, COLOMBIA. (Sp.) Llanos, G. (Nat. U. Colombia, Bogota), P. Correa and O. Barbosa. *Antioquia Med.* 19(5):377-388, 1969.

In Cartagena, Colombia, the incidence of cancer/100,000 population in 1966 was 73.6 for males and 92.3 for females. Most frequent among males (number/100,000 population, as above) were cancers of the prostate, lungs and bronchi, skin (excluding melanomas), and bladder (12.0, 8.3, 8.2 and 7.4, resp.) followed by cancers of the stomach, rectum, liver, penis, or testis (2.8 each) and by Hodgkin's disease, leukemia, lymphosarcoma and reticulum cell sarcoma (combined), and cancers of the soft tissues (2.7 each). Most frequent among females were cancers of the cervix, other uterine sites, ovary, other genital sites, breast, skin (excluding melanomas), and bladder (26.5, 27.2, 24.0, 24.0, 11.2, 8.8 and 4.8, resp.) and stomach, pharynx, or buccal cavity (2.4 each). In general, extragenital cancers were more common among males and the degree of risk, for both males and females, increased progressively with advancing age, with very sharp increases at ages 30-39 yr. and 40-49 yr.

70-330 NASOPHARYNGEAL CANCERS IN VIETNAM: EPIDEMIOLOGY, CLINICAL ASPECTS, POSSIBLE ETIOLOGIC FACTORS. (Fr.) Huong, B.-Q. (Inst. Cancer, Saigon), N. P. Buu-Hoï, P.-N. Duong, N.-H. Te and D.-D. Hoang. *Ann. Otolaryng.* (Paris) 86(4-5):267-278, 1969.

A total of 393/4439 cancers seen in a Saigon hospital during the yr. 1961-1963, inclusive, were cancers of the upper digestive or respiratory tracts; 163/393 were nasopharyngeal cancers, with a male:female ratio of 105:58. Of 132 studied histologically, 7 were lymphosarcomas (all occurring in young adults), 29 were spinocellular carcinomas, 3 were glandular carcinomas, 20 were basal cell carcinomas and 73 were mixed carcinomas. Only 6/163 pts. were Chinese; the rest were Vietnamese. There were no pts. under 20 yr. of age. The peak frequency of occurrence was between 40-49 yr. of age. Metastatic lymphadenopathies were demonstrable in 75% of the pts.; trigeminal neuralgia, facial paralysis and middle ear deafness, in 13%; lesions of 1 or more cranial nerves in 120/163; other neurologic complication in 55/163. The indicated incidence of 3.6 cases/100,000 population/yr. was approximately the same as that for Malaysians and Thais (2.4/ and 3.0, resp.); lower than that for Indonesians (6.5) significantly lower than that for Chinese (not stated); and significantly higher than that for Indians, Japanese, or Caucasians (not stated). A strong genetic influence is postulated, supplemented by the co-carcinogenic effects of a nutritional deficiency of Vitamin A, the habit of making a noisy, violent movement of the pharynx before expectorating, the habit of retaining tobacco smoke in the

buccal cavity and then expelling it through the nose, and the habit of regularly inhaling certain aromatic oils or applying them intranasally as treatment for and prophylaxis against g.i. tract and respiratory disorders.

70-331 A HISTOLOGICAL STUDY OF CHROMATIN POSITIVE AND NEGATIVE HYDATIDIFORM MOLES. (E.) Loke, Y. W. (U. Cambridge, England) and R. Borland. *Brit. J. Cancer* 23(3):554-558, 1969.

In a histological study of 105 spontaneously aborted hydatidiform moles, 13 hydatidiform moles with uterine removal, 7 uterine choriocarcinomas, 1 fallopian tube carcinoma, and 1 ovarian mole, trophoblastic proliferation was most often seen in chromatin-positive moles. Markedly proliferative moles penetrated deeply into uterine muscle. Decidual reaction was seen in all except 2 moles and lymphocytic infiltration and fibrinoid degeneration of small blood vessels was present around molar tissue in half the cases. Decidual reaction and lymphocytic infiltration were present in both hydatidiform moles and uterine choriocarcinoma, but there were no giant cells or fibrinoid necrosis in the choriocarcinomas.

70-332 PATHOGENETIC, EPIDEMIOLOGIC AND HISTOPATHOLOGIC ASPECTS OF PHAGEDENIC ULCERS AND THEIR CARCINOGENESIS. (A STUDY OF COMPARATIVE CARCINOGENESIS.) (Fr.) Serafino, X., Y. Nosny and P. A. Menye. *Bull. Soc. Path. Exot.* 62(3):618-634, 1969.

A total of 235/457 carcinomas of the skin seen at the Dakar Cancer Institute between 1962-1968, inclusive involved carcinogenesis of phagedenic ulcers. The frequency with which such carcinogenesis occurred was estimated at 10-15%, with a mean latent period of 18-24 mo. There were no significant age or sex differences, although all of the pts. were adults or young adults (age range, 17-80 yr.). Ninety percent of the pts. with phagedenic ulcers were farm workers. The most frequent sites of ulceration were the foot, ankle, and heel, and ulceration was almost invariably accompanied by contact osteolysis, contact osteitis, or both. The most frequent type of cancer developing at the site of a phagedenic ulcer was a spinocellular carcinoma, identical with the type which develops at the site of a burn or a radiation lesion. Severe osteoperiostitic lesions were found in 52/235 pts. with cancer at the site of an ulcer; 105/235 showed such destructive osseous lesions as osseous rarefaction at a distance, true osteitic lesions, necrosing osteomyelitis, or destructive metastatic invasion of the bone. Although 134/155 pts. who were examined showed inguino-crural lymphadenopathy, only 39/128 which were studied histologically proved to be malignant. Among all pts. showing carcinogenesis at the

site of a phagedenic ulcer, only 12/235 showed evidence of distant metastases, with 11/12 dying within less than 1 yr. after their appearance. Included is a brief review of the etiology of phagedenic ulcers. The author estimates that cancers occurring at the site of such ulcers account for more than 10% of all malignant tumors seen in East Africa.

- 70-333 THE GROWTH CURVE OF THE RAT THYROID UNDER A GOITROGENIC STIMULUS. (E.) Philp, J. R. (Univ. Med. Sch., Aberdeen, Scotland), J. Crooks, A. G. Macgregor and J. A. R. McIntosh. Brit. J. Cancer 23(3):515-523, 1969.

Male Wistar rats were allowed to drink a 0.1% soln. of methylthiouracil (M) in 1% sucrose ad libitum and were sacrificed from 0-36 days after the start of the experiment. Controls received only sucrose. A three-part growth curve for thyroid weight was described for animals ingesting M: an initial 2-day lag phase; a 10 day exponential phase; and a plateau phase. The total thyroid follicular cell population underwent a pattern of increase identical to that for gland wt. The authors suggest that the exponential reproduction of follicular cells under goitrogenic stimulus provides a mode for quantitative studies of drugs affecting cell division in vivo.

- 70-334 AMINO ACIDS AS STIMULATING AGENTS OF DNA-REPLICATION IN MELANOMAS. I.

STIMULATION IN EXPLANTS. (E.) Anders, F. (Justus Liebig U., Genet. Inst., Giessen, Germany), M. Sieger and K. Klinke. Experientia 25(8):871-874, 1969.

This study presents observations on the pterinophore gene Dr (dorsal red) and the macromelanophore gene Sd (spotted dorsal), which are closely linked on the X chromosome of the wild species (Platyopocilus maculatus) of platy-fishswordtail hybrids. One half of each explant of Dr-Sd melanomas was incubated in a fish tissue culture (medium 199 and calf serum), in which the level of free amino acids was less than that in the tumors; the other half was incubated in the same medium with added amino acids. ³H-thymidine was added and labeling indices determined. Results showed that amino acids have the ability to stimulate replication of DNA in melanoma cells. Excessive stimulation of DNA was seen only in the absence of the repressor gene RGDrsd, which specifically repressed the Dr and Sd genes. It is concluded that tumor formation depends on 2 separate events: derepression of cell-determining genes and stimulation of replication in cells which they determine.

- 70-335 ENDOCRINOLOGY AND EPIDEMIOLOGY OF BREAST CANCER. (E.) MacMahon, B. (Harvard Sch. Pub. Health., Boston, Mass.) and P. Cole. Cancer 24(6):1146-1149, 1969.

See also abstract nos.: 172,179,296,304,316,338

70-336 FAMILIAL MULTIPLE POLYPS OF THE COLON. (Pol.) Szklanny, J. (Acad. Med., Lodz, Poland) and M. Kun. Pol. Tyg. Lek. 24(25): 967-969, 1969.

The occurrence of familial polyposis is described in a family of 13. Diffuse multiple polyps of the colon were discovered in 6 members of this family, (2 females, 4 males) 2 of whom (both males) subsequently died of carcinoma (solid adenocarcinoma and mucinous papillary adenocarcinoma). Two grandparents had also died of intestinal neoplasms (no further details). In 5, no abnormalities were found. It is suggested that there seems to be a relationship between number of polyps and neoplastic change. Immediate complete resection of the large intestine is recommended in young patients with a history of familial polyposis.

70-337 ACUTE MYELOGENOUS LEUKEMIA IN THE COURSE OF SYSTEMIC LUPUS ERYTHEMATOSUS. (Pol.) Jochweds, B. (Tuberc. Inst., Warsaw), E. Szulkin and Z. Kamiński. Pol. Arch. Med. Wewnet. 42(4):693-697, 1969.

A case history is presented of a 64-yr.-old woman with systemic lupus erythematosus who had been treated with increasing doses of cortisone (up to 80 mg/day) for 6 mo. before developing acute myelogenous leukemia. She died 3 mo. later. Autopsy revealed extensive collagenosis frequently coexisting with leukemic infiltration in many organs (lungs, liver, spleen, lymph nodes, cardiac muscle) and typical leukemic changes in the bone marrow. Possibility of a common pathogenesis of both conditions is briefly discussed.

70-338 THE ASSOCIATION BETWEEN SALIVARY GLAND CANCER AND BREAST CANCER. (E.) Moertel, C. G. (Mayo Clin., Rochester, Minn.) and L. R. Elveback. JAMA 210(2):306-308, 1969.

In a group of 297 women with carcinoma of the major salivary glands (parotid and submaxillary) followed-up for a total of 3,033 pt.-yr., 4 developed breast adenocarcinoma. This incidence does not exceed the expected norms, therefore no association is indicated between these two neoplasms.

70-339 FREQUENCY OF MALIGNANT TRANSFORMATION IN FIBROUS DYSPLASIA OF BONE. (Pol.) Buraczewski, J. (Inst. Oncol., Warsaw) and J. Dziukowa. Nowotwory 19(1):15-28, 1969.

Five cases of histologically confirmed malignant transformation and 7 in which dysplasia was not fully confirmed are presented. The first group included 4 women (17, 23, 29 and 49 yr. old) and

1 man (55 yr.). Dysplasia was oligosteitic in 1, monoosteitic and in 1 and local in 3 cases. Histologically 2 were fibrosarcomas, 1 chondrosarcoma, 1 fibrochondrosarcoma, 1 undefined. The femur was involved in 2, jaw in 1, tibia in 1 and humerus in 1 case. The second group included 4 females (11, 12, 13 and 63 yr. old) and 3 males (3, 16 and 55 yr. old). Dysplasia was monoosteitic in 2, oligosteitic in 1, generalized in 1 and local in 3 cases. The femur was affected in 3, tibia in 2, jaw in 1 and humerus in 1 case. Histologically 2 were fibrosarcomas, 1 chondrosarcoma, 1 osteogenic sarcoma, 1 osteoclastoma and 1 anaplastic tumor. In addition to these cases, 30 reported in the literature are tabulated. Dysplastic changes were also seen by the authors in 30/539 (5.5%) of cases with malignant bone tumors. These included 7/55 (12.7%) fibrosarcomas, 13/90 (14.3%) chondrosarcomas and 6/141 (4.3%) osteosarcomas. It is concluded that malignant transformation of fibrous dysplasia occurs more frequently than is generally assumed and that foci of fibrous dysplasia should be regarded as potentially dangerous, carefully followed and possibly subjected to radical surgery.

70-340 FOLLICULAR HYPERPLASIA IN LYMPH NODES FROM PATIENTS WITH RHEUMATOID ARTHRITIS. A CLINICOPATHOLOGIC STUDY. (E.) Nosanchuk, J. S. and B. Schnitzer (1335 E. Catherine St., Ann Arbor, Mich.). Cancer 24(2):343-349, 1969.

Follicular hyperplasia and plasmacytosis were the most outstanding features at lymph node biopsy in 13 men and 8 women (30-64 yr. old) with rheumatoid arthritis. Neutrophils were seen in the sinuses and lymphocyte infiltration of the capsule and perinodal fat, with proliferation of the vascular endothelium was frequent. An abundance of plasma cell infiltration was seen in lymph nodes examined at autopsy in 11 men and 10 women (12-86 yr.) with a decrease in follicular particles as compared to surgical biopsies.

70-341 ULTRASTRUCTURE OF A BURKITT'S LYMPHOMA MARKER CHROMOSOME, AS INVESTIGATED BY QUANTITATIVE ELECTRON MICROSCOPY. (E.) Lampert, F., G. F. Bahr (Armed Forces Inst. Path., Washington, D. C.) and E. J. DuPraw. Cancer 24(2):367-376, 1969.

Burkitt's lymphoma cells obtained from the jaw tumor of a 7-yr.-old boy and serially propagated in suspension culture, had chromosome numbers ranging from 44-52, and 2-3 marker chromosomes. The structure of the marker chromosomes was twisted fibers about 300 Å in diameter. The large marker chromosome was in close proximity to the medium and small acrocentric chromosomes, and connected to 13-15 chromosomes by common fibers.

70-342 POSSIBLE DIFFERENCES BETWEEN THE KARYOTYPES OF PREINVASIVE LESIONS AND MALIGNANT TUMOURS. (E.) Atkin, N. B. (Mt. Vernon Hosp., Northwood, Middlesex, England) and M. C. Baker. Brit. J. Cancer 23(2):329-336, 1969.

The relative number of chromosomes in D and G groups was usually below the expected number in 23 tumors (choriocarcinoma, corpus uteri, ovary, breast, colon, rectum, bladder, skin, testis), and the B group chromosomes were always below the expected value. Similar results were seen in 11 carcinomas of the cervix. In 14 preinvasive lesions of the cervix, however, a small excess of G group chromosomes and about the expected number of D group chromosomes were seen; the B group was a little below the expected number. In rectal polyps, the B group was slightly lower than normal and the D and G groups slightly higher. In a series of 20 ovarian carcinomas the modal chromosome number was < 46 in 4, and ranged from 48-81 in the others; 19/20 had marker chromosomes.

70-343 SYSTEMIC EFFECT OF MOUSE LEUKEMIA ON RNASE AND ITS INHIBITOR OF HOST LIVER AND SPLEEN. (E.) Nagao, M. (Nat. Cancer Ctr. Res. Inst., Tokyo) and Y. Ichikawa. Gann 60(3):279-285, 1969.

RNase and inhibitor of alkaline RNase were assayed on C-1498 leukemia cells of C57BL/6 mice, SN-36 leukemic cells of dds mice (both leukemia strains inj. i.p. 7 days before sacrifice), and on their liver and spleen. RNase activities of C-1498 and SN-36 cells were much lower than those of liver or spleen. RNase activity decreased in liver and spleen of C-1498-bearing mice but increased somewhat in those SN-36-bearing mice. Higher titers of inhibitor were found in livers of C57BL/6 mice than dds mice; C-1498 cells had much less inhibitor titer than SN-36 cells. Determination of spleen RNase inhibitor titer was relatively the same for both strains of mice. Compared to normals, there was a definite decrease and a definite increase in RNase inhibitor titer for C-1498-bearing C57BL/6 mice and SN-36-bearing dds mice, resp. It was concluded that there is a different systemic effect on host liver by different strains of leukemia.

70-344 ISOENZYMES OF GLUTAMATE-OXALACETATE-TRANSAMINASES IN TUMOURS. (E.) Allen, J. (Oncol. Inst., Bratislava, Czechoslovakia) and A. Hrivňáková. Arch. Geschwulstforsch. 3(4):350-355, 1969.

Electrophoresis on cellulose acetate foil was used to fractionate the glutamate-oxalacetate-transaminases (GOT) in sera and in normal and tumor tissue into isoenzymes: the slow moving, microsomal cathodic fraction and the soluble

cytoplasmatic which moves towards the anode. In normal sera only the cytoplasmic isoenzyme was present while tissue homogenates always showed 2 fractions. The anodic fraction, whether from normal or malignant tissues, always moved faster, animal slower than human (except for human embryo). Mixtures of tissue homogenates and serum showed 3 fractions indicating a structural difference in the anodic fraction. The electrophoretic mobility of transaminases from cancer tissues were identical to normal tissues, but there was a slight increase in percent activity of cathodic fraction in malignant tissue. The glutamic-oxalacetic transaminase (GOT) activity in cancer pt. serum showed no relationship to size or stage of tumor. Pts. with tumor showing high cathodic GOT activity did not have this fraction in peripheral blood. This is in contrast to observations made in cases of liver disease and it is suggested that the "tumor" GOT with slow electrophoretic mobility differs from the hepatic microsomal fraction in this regard.

70-345 GROWTH AND GLUCOSE METABOLISM OF HIGH AND LOW TUMOR-PRODUCING CLONES UNDER AEROBIC AND ANAEROBIC CONDITIONS IN VITRO. (E.) Sanford, K. K. (NCI Biol. Lab., Bethesda, Md.) and B. B. Westfall. J. Nat. Cancer Inst. 42(6):953-959, 1969.

Glucose uptake, and lactic acid production, and growth were studied in vitro under aerobic and anaerobic conditions in high tumor-producing (NCTC 2472) and low tumor-producing (NCTC 2555 and NCTC 2445) mouse clones. All clones apparently metabolized glucose similarly during aerobic growth. In static cultures, there was an inverse relationship between inoculum size and rate of glycolytic flux during the lag and early log phases of growth, followed by a decrease to a low rate during late log and stationary phases. Under anaerobic conditions for 72 hr., mitosis was suppressed in all clones and glucose uptake and lactate accumulation were significantly increased. However, lactate in the medium accounted for only 50% of the glucose taken up.

70-346 EFFECTS OF CHANGING HORSE AND FETAL CALF SERUM SUPPLEMENTS ON NEOPLASTIC CONVERSION AND CHROMOSOMAL CHARACTERISTICS OF MOUSE EMBRYO CELLS IN VITRO. (E.) Andresen, W. F. (U. Nebraska, Lincoln), J. L. Jackson, J. T. Mitchell and V. J. Evans. J. Nat. Cancer Inst. 43(2):377-383, 1969.

In cell lines of C3H/HeN mouse embryo cells established in vitro in NCTC 135 medium containing horse serum (HS; 10%) or fetal calf serum (FCS; 10%) with serum supplements changed at 15, 60 and 90 days, cells exposed to HS x 15 days were irreversibly neoplastically converted, even though they were changed to FCS for

continuous growth. Cells initiated in FCS and changed to HS for continuous growth also became converted. Cells that became neoplastically converted produced tumors at inj. sites in young, male syngeneic animals. Cells initiated and maintained in FCS were not converted. No correlation was seen with neoplastic changes and chromosomal characteristics of cells before and after serum changes.

- 70-347 STABILITY IN VITRO OF DIVERSE CAPACITIES FOR TUMOR PRODUCTION AND GLUCOSE METABOLISM IN THREE MURINE CLONES DERIVED FROM THE SAME CELL. (E.) Sanford, K. K. (NCI Biol. Lab., Bethesda, Md.), M. W. Woods, D. B. M. Scott and H. A. Kerr. J. Nat. Cancer Inst. 42(6): 945-952, 1969.

After 6-7 yr. of in vitro growth cells of 3 clones (high tumor-producing NCTC 2472 and low tumor-producing NCTC 2555 and 2445), growing in a horse serum-supplemented medium, were tested for tumorigenicity after i.m. inj. in untreated and X-irradiated C3H mice. In untreated hosts, clone 2472 produced a significantly higher number of tumors with shorter latent periods, than did clones 2555 or 2445; the latent period was shorter with 2555 than with 2445. In X-irradiated hosts (425 r 4 hr. before cell inoc.), the tumor incidence was increased with all 3 clones. A higher incidence and shorter latency was seen with 2472; the incidence with 2555 was slightly higher than with 2445. Derivatives of these clones grown in chemically defined medium seemed to produce tumors from smaller cell numbers than the parent clones in serum-supplemented medium. The anaerobic glycolytic capacities of the parent clones were similar to those reported originally 8 yr. before and correlated well with in vivo growth characteristics. The results show that immune suppression of cell growth in vivo plays an important role in determining initiation of tumor development and latent periods for cells carried in the presence of horse serum. There was some correlation between glycolytic capacity and in vivo tumor production in derivative strains of low tumor-producing parent clones.

- 70-348 CULTIVATION IN VITRO OF CELLS DERIVED FROM ADULT C3H MOUSE VENTRAL PROSTATE. (E.) Chen, T. T. (Indiana U. Med. Ctr., Indianapolis) and C. Heidelberger. J. Nat. Cancer Inst. 42(6):903-914, 1969.

Eight cell lines were derived from organ cultures of C3H mouse ventral prostate and maintained in either Eagle's basal essential medium (BME) plus 10 or 20% fetal calf serum (FCS) (7 lines) or NCTC 109 medium plus FCS (1 line). Cell lines appeared initially epithelial, in comparison with the fibroblast-like nature of primary cultures made directly from mouse prostate. All cell lines reached a saturation

density when a monolayer had formed and they did not pile up. Cultures plated at high density (B2, B3) were epithelial-like, compared with smaller, fibroblast-like cells derived from lower density cultures (B4, B5). Cells of the latter 4 lines were inoc. s.c. into C3H adult males 2 days after radiation (400-500 r) of the mice. B2 produced no tumors through 211 days in culture, but produced fibrosarcomas in 2/3 mice inj. after 261 days in culture, showing the occurrence of spontaneous malignant transformation in these cells. No tumors were induced by cells of either B3 or B4, grown for 137 days, nor by B5 cells grown for 265 days. Spontaneous malignant transformation was seen between days 188-344 of culture in the cell line grown in NCTC 109 medium. In all cases, cells developed the ability to produce tumors at the same time they piled up. All cell lines were aneuploid by the 20th subculture.

- 70-349 FINE STRUCTURE OF MURINE MAMMARY TUMOURS: THE RELATIONSHIP BETWEEN EPITHELIUM AND CONNECTIVE TISSUE IN NEOPLASMS INDUCED BY VARIOUS AGENTS. (E.) Tarin, D. (U. Leeds Sch. Med., England). Brit. J. Cancer 23(2):417-425, 1969.

In C3H mice with virus-induced mammary tumors, C57 mice with spontaneous mammary tumors and (C57BL x 1F)₁ virgin female mice with methylcholanthrene (MC; cutaneous treatment every 2 weeks for 8 occasions)-induced mammary tumors, similar structural changes were seen in the tumors at the epithelio-mesenchymal junction. Accumulation of fragmented material in the connective tissue close to the basement membrane and grossly disorganized connective tissue were the most prominent changes. In MC-induced tumors a marked myoepithelial cell proliferation was observed.

- 70-350 METASTATIC GANGLIONEUROBLASTOMA. ULTRASTRUCTURAL, HISTOCHEMICAL, AND VIROLOGICAL STUDIES IN A CASE. (E.) Beltran, G. (Tulane U. Sch. Med., New Orleans, La.), E. Leiderman, W. J. Stuckey, V. J. Ferrans and W. J. Mogabgab. Cancer 24(3):552-560, 1969.

Lymph nodes removed from a 3-yr.-old girl after surgical removal of a ganglioneuroblastoma and after chemotherapy, were composed largely of polyhedral tumor cells with great numbers of cytoplasmic processes filling the spaces between cells. Intense fluorescence was seen in lymph node cells exposed to paraformaldehyde suggesting the presence of catecholamines. Very few intact cells were found in bone marrow aspirants, but elements similar to the cytoplasmic processes above were plentiful. No viral activity was observed after inoc. of tumor tissue into cell cultures, hemagglutination, or complement fixation studies.

AUTHOR INDEX

- Adamiker, D. 211
 Adenis, L. 238
 Alexandrescu, M. 306
 Allison, A. C. 281
 Altenbrunn, H.-J. 169
 Altman, R. F. A. 198
 Altmann, H. 211
 Anders, F. 334
 Andresen, W. F. 346
 Aoyama, Y. 304
 Arcos, J. C. 191,199
 Argus, M. F. 191,199
 Atkin, N. B. 342
 Auerbach, O. 178
 Aya, T. 317

 Ba Giao, N. 206
 Bahr, G. F. 341
 Baker, L. A. 265
 Baker, M. C. 342
 Baldwin, R. W. 203,245
 Ballini-Kerr, I. 198
 Banerjee, M. R. 292
 Barbosa, O. 329
 Beltran, G. 350
 Berlie, J. 328
 Berman, L. D. 281
 Berry, G. 183
 Biquard, J.-M. 269
 Biriulina, T. I. 278
 Borland, R. 331
 Börner, P. 195
 Botkin, C. 252
 Bremberg, S. 300
 Brodsky, I. 261
 Brookes, P. 232
 Brown, J. 241
 Brunet, M. 328
 Bubeník, J. 280
 Bucz, B. 322
 Buraczewski, J. 339
 Burki, H. R. 210
 Butler, W. H. 185
 Buu-Hoi, N. P. 330

 Calvoer, R. 244
 Cappelaere, P. 238
 Carasievici, E. 306
 Carter, R. L. 233
 Chamorro, A. 264
 Chen, T. T. 226,348
 Chermann, J.-C. 266
 Chevalier, H.-J. 207
 Chirico, G. 326
 Chirigos, M. A. 270
 Chopra, H. C. 293
 Christian, I. 222,223,224
 Cioloca, L. 221
 Claude, A. 307
 Colby, C. 276
 Cole, P. 335
 Correa, P. 329

 Cox, B. 197
 Crooks, J. 333

 Daniel-Moussard, H. 181
 Dannenberg, H. 246
 Davidson, J. K. 182
 Dehnen, W. 205
 Delange, J. 189
 DeLong, D. C. 265
 DeOme, K. B. 286,289
 Dessev, G. N. 201
 de Vaux Saint Cyr, C. 313
 d'Hooghe, M. 238
 Dickie, M. M. 250
 Dillard, R. D. 265
 Dimitrov, N. V. 261
 Dipple, A. 232
 Dmochowski, L. 294
 Domschke, W. 194
 Donner, L. 280
 Dontenwill, W. 174,175,176,
 180,207
 Driessens, J. 238
 Dubbs, D. R. 315
 Duca, M. 306
 Duncan, M. 232
 Dunn, J. A. 202
 Duong, P.-N. 330
 DuPraw, E. J. 341
 Durif, S. 181
 Dutrillaux-Ducros, M.-C. 287
 Dziukowa, J. 339

 Easton, N. R. 265
 Ehrentraut, W. 249
 Elmenhorst, H. 174,175,176
 Elveback, L. R. 338
 Encut, I. 221
 Epstein, A. 300
 Epstein, S. S. 164
 Evans, C. A. 308
 Evans, V. J. 346

 Fadda, G. 279
 Fasske, E. 311
 Fehr, P.-M. 189
 Feller, W. F. 293
 Feiluga, B. 307
 Ferrans, V. J. 350
 Fetting, R. 311
 Fey, F. 263
 Fichidzhian, B. S. 273
 Fischinger, P. J. 272
 Flowers, A. 320
 Fraumeni, J. F., Jr. 316
 Friedrich-Frekso, H. 195
 Frischauf, H. 211
 Fukuoka, F. 229

 Gadekar, K. 252
 Galea, V. 161
 Gallager, H. S. 294
 Gallina, F. 326
 Garfinkel, L. 178
 Garrett, T. 209
 Gerardi, A. 327
 Gerwel, T. 172
 Gibel, W. 162,163
 Glover, E. L. 213
 Gold, E. 316
 Goodall, C. M. 185
 Goodman, E. S. 303
 Gosch, H. H. 199
 Gössner, W. 195
 Grabar, P. 313
 Granados, R. R. 321
 Grosso, E. 325
 Gruenstein, M. 212

 Hagopian, M. 173
 Hammond, E. C. 178
 Hancock, R. L. 250
 Handrache, L. 306
 Harke, H.-P. 174,175,176,180
 Hartenstein, R. 204
 Hecker, E. 208
 Heidelberger, C. 226,348
 Hellström, I. 308
 Hellström, K. E. 308
 Hems, G. 179
 Henry, M. 287
 Herrold, K. M. 187
 Hiasa, Y. 243
 Hinuma, Y. 296
 Hiraki, K. 260
 Hirokawa, Y. 268
 Hirose, F. 167
 Hirschman, S. Z. 272
 Hirumi, H. 321
 Hoang, D.-D. 330
 Hollande, E. 287
 Hollmann, K. H. 291
 Hopewell, J. W. 234
 Horn, D. 166
 Hoshino, H. 229
 Howard, B. V. 314
 Howell, B. A. 197
 Hrivňáková, A. 344
 Hueper, W. C. 241
 Huggins, C. 220,246
 Hulse, E. V. 168
 Huong, B.-Q. 330

 Ichikawa, Y. 343
 Ichimura, H. 251
 Ikawa, Y. 268
 Imaeda, Y. 267
 Imaizumi, T. 192,196,248
 Inbar, M. 312
 Ionescu, L. 306
 Irino, S. 260

- Ishii, K. 304
 Ishizawa, J. 230
 Ito, N. 243
 Ito, Y. 267,298,302
- Jackson, J. L. 346
 Jänisch, W. 242,253
 Jasmin, C. 266
 Jellinck, P. H. 209
 Jochweds, B. 337
 Juhls, H. 249
 Jull, J. W. 216,217,218
- Kalinovsky, T. 288
 Kamiński, Z. 337
 Kato, H. 317
 Kato, R. 186
 Katz, C. 237
 Kawamura, A., Jr. 304
 Kawazoe, Y. 229
 Kellen, J. 344
 Kellner, G. 211
 Kelly, M. G. 252
 Kerr, H. A. 347
 Kew, M. C. 202
 Kit, S. 315
 Kizer, D. E. 197
 Klein, G. 300,301
 Klink, K. 334
 Knorre, D. 235
 Kolbye, A. C. 166
 Koldovsky, P. 279
 Kolompár, G. 322
 Kondo, M. 251
 Kosuge, T. 259
 Kovács, E. 322
 Kovács, K. 219
 Koyama, K. 304
 Krishan, A. 320
 Kritchevsky, D. 314
 Kriukova, I. N. 277,278
 Krüger, F. W. 247
 Kühn, B. 169
 Kumkumadzhian, V. A. 273
 Kun, M. 336
 Kunz, W. 236
 Kunze, E. 244
 Kupfer, G. 249
 Kupfer, M. 249
 Kurimura, T. 315
 Kuroki, T. 230
 Kuznetsova, N. N. 278
- Lacassagne, A. 206
 Lafrenz, U. 180,207
 Lampert, F. 341
 Lauenstein, K. 262
 Le Bouffant, L. 181
 Lee, K. P. 309
 Leiderman, E. 350
 Lepow, M. L. 316
 Liciu, F. 221
 Lijinsky, W. 164
- Liu, P. I. S. 303
 Llanos, G. 329
 Loke, Y. W. 331
- Macgregor, A. G. 333
 MacMahon, B. 335
 Macpherson, P. 182
 Mallet, R. C. 202
 Maramorosch, K. 321
 Martin, J.-C. 181
 Mathé, G. 266
 Mathison, J. B. 191
 Matthes, T. 169
 Matusuyama, M. 215
 Maujol, L. 328
 Mazzola, S. 327
 Mazzucco, K. 222,223,224
 McIntosh, J. A. R. 333
 Medina, D. 286,289
 Melchionne, S. 237
 Menye, P. A. 332
 Meranze, D. R. 212
 Merkow, L. P. 305
 Merwin, R. M. 283
 Meyer-Bertenrath, J. G. 194
 Mickelsen, O. 240
 Miller, G. F. 285
 Misfeld, J. 174,175,176
 Mitchell, J. T. 346
 Miyaki, K. 257
 Miyoshi, I. 260
 Moertel, C. G. 338
 Mogabgab, W. J. 350
 Mole, R. H. 168
 Moore, M. 203
 Mori, K. 251
 Morton, D. L. 285
 Mouriquand, C. 290
 Mouriquand, J. 290
 Mrena, E. 307
 Mullock, B. M. 201
 Muramatsu, M. 200
- Nagao, M. 343
 Nagao, T. 260
 Napalkov, N. P. 231
 Newberne, P. M. 188
 Nishimura, R. 239
 Nishioka, K. 304
 Normand, C. 181
 Nosanchuk, J. S. 340
 Nosny, Y. 332
- Oboshi, S. 299
 Obukh, I. B. 277,278
 O'Connor, T. E. 272
 O'Gara, R. W. 241,252
 Ogawa, K. 256
 Ohta, A. 251
 Okano, T. 227,228
 Okita, G. T. 210
 Oliverio, V. T. 252
 Olson, C. 309
- Olson, R. 288
 Omori, Y. 186
 Onoé, T. 256
 Onoka, K. 186
 Osato, T. 297,298
 Osske, G. 242
- Pardo, M. 305
 Pasternak, G. 263,271
 Pasternak, L. 271
 Paul, D. 208
 Petrova, N. V. 255
 Phillips, A. J. 216
 Philp, J. R. 333
 Pinkerton, H. 303
 Pipkin, G. E. 239
 Pokorný, J. 311
 Policard, A. 181
 Pong, R. S. 190
 Popescu, N. C. 221
 Pozharisski, K. M. 231
 Preda, N. 161
- Rabes, H. 204
 Rabinowitz, Z. 312
 Rapoza, N. P. 305
 Raychaudhuri, R. 320
 Reckzeh, G. 174,175,176,
 180,207
 Redmon, L. W. 283
 Reid, E. 201
 Reuber, M. D. 213
 Reynaud, M. 266
 Rogers, A. E. 188
 Romeril, M. G. 245
 Rosenkrantz, H. 173
 Roth, D. 170
 Rothwell, K. 177
 Rubin, H. 276
 Rudolph, R. 282
- Sachs, L. 312
 Sage, H. H. 170
 Sakiyama, H. 275
 Sambrook, J. 318
 Sandberg, A. A. 317
 Sanford, K. K. 345,347
 Sanger, V. L. 240
 Sato, H. 230
 Sato, Y. 228
 Sawanishi, H. 259
 Schabert, J. C. 184
 Schäfer, A. 295
 Schade, G. 236
 Schauer, A. 244
 Scherbaum, O. H. 211
 Schlegel, J. U. 239
 Schmöhl, D. 247
 Schneider, J. 242
 Schnitzer, B. 340
 Scholes, V. E. 225
 Scholze, P. 204
 Schramm, T. 162,163

Schreiber, D. 242,253
 Schultz, G. N. 239
 Schwenke, K.-D. 193
 Scott, D. B. M. 347
 Scribner, J. D. 165
 Seidel, H. J. 262
 Seilern-Aspang, F. 222,223,224
 Seman, G. 294
 Serafino, X. 332
 Sevoian, M. 319
 Shatkin, A. J. 318
 Shikata, E. 321
 Shimizu, M. 258
 Shimkin, M. B. 212
 Shimojo, H. 304
 Shiratori, O. 267
 Shirley, B. C. 197
 Sieger, M. 334
 Sikorowa, L. 171
 Šimkovič, D. 284
 Šimkovičová, M. 284
 Sims, P. 214
 Sivak, A. 237
 Slifkin, M. 305
 Somogyi, A. 219
 Stark, C. R. 316
 Stavrou, D. 254
 Stewart, L. 241
 Steyn, M. 184
 Tuckey, W. J. 350
 Ugano, H. 268
 Ugawara, K. 297
 Uzuki, H. 215
 Uzuki, Y. 259
 Zklanny, J. 336
 Zulkan, E. 337

Taguchi, E. 227
 Takagi, N. 317
 Takahashi, T. 267
 Takata, H. 260
 Takayama, S. 192,196,
 200,248
 Takenaka, S. 228
 Takeuchi, M. 274
 Tamai, A. 243
 Tamura, M. 251
 Tarin, D. 349
 Tausch, H. 253
 Taylor, J. D. 202
 Te, N.-H. 330
 Terao, K. 257
 Themann, H. 311
 Thomas, C. 236
 Thomas, J. A. 287
 Thurzo, V. 284
 Tilz, G. P. 313
 Timm, J. 174,175,176
 Tomingas, R. 205
 Tsubota, T. 260
 Turano, A. 279,280
 Turner, M. K. 201
 Turner, W. 270

Uekama, K. 227
 Uematsu, K. 220

Vaage, J. 288
 Van Duuren, B. L. 237
 Verley, J. M. 291
 Viala, C. 290

Wagner, J. C. 183
 Walker, R. 323,324
 Warzok, R. 253
 Watrach, A. M. 310
 Weber, K. H. 174,175,176
 Weiss, E. 282
 Westfall, B. B. 345
 Wheatley, D. N. 214
 Whitehead, J. K. 177
 Wogan, G. N. 190
 Wood, D. A. 285
 Woods, M. W. 347
 Wright, E. A. 234

Yamaguchi, N. 274
 Yamamoto, K. 297
 Yamamoto, T. 274
 Yancey, S. T. 252
 Yang, M. G. 240
 Yata, J. 301
 Yoshida, K. 243
 Yoshida, T. O. 302
 Yoshikura, H. 268

Zacharia, T. P. 319
 Zenda, H. 259
 Zil'fian, V. N. 273
 Zintzsch, I. 249
 Zuccari, F. M. 326

SUBJECT INDEX

- ACETAMIDE, THIO-
 hepatoma, ribosomal proteins, rat: 194
- ACRIDINE, 3,6-BISDIMETHYLAMINO- (acridine orange)
 skin tumors, mouse: 237
- ADRENAL NECROSIS
 dimethylbenzanthracene, rat: 214
 metopirone and Su-4885 metabolism: 209
 7-hydroxymethyl-12-methylbenzanthracene, rat: 214
- AFLATOXIN(S)
 effect on liver, chick embryo: 257
 kidney, g.i. and liver tumors, hamster: 187
 hepatoma, effect of hypophysectomy, rat: 185
- AFLATOXIN B-1
 effect on
 cholesterol synthesis, rat liver: 186
 dimethylbenzanthracene ovarian tumors, mouse: 218
 fermentation of cellulose, rumen preparation *in vitro*: 189
 liver polysomes, rat: 190
 hepatoma, effect of lipotrope deficiency, rat: 188
 metabolism, liver, rat: 184
- AGE FACTORS
 dimethylbenzanthracene carcinogenesis, rat: 212
 leukemia, mouse: 220
- AIR POLLUTION
 benzpyrene, coke plant, USSR: 255
- AMINO ACIDS
 aromatic, interaction with nitroquinoline oxide, mechanism: 228
- ANTHRANILIC ACID, 3-HYDROXY- (tryptophan metabolite)
 bladder tumors, effect of ascorbic acid, mouse: 239
- ANTITUMOR AGENTS
 acetylenic carbamate type, effect on Friend virus leukemia, mouse: 265
 actinomycin or cycloheximide, effect on dimethylbenzanthracene ovarian tumors, mouse: 218
 bleomycin, effect on nucleus, methylcholanthrene-induced skin tumor, mouse: 256
 cytosine arabinoside, effect on Moloney or Rauscher virus *in vitro*: 272
 ibenzmethylzin, lung tumors, mouse: 252
- ASBESTOS
 detection, asbestosis: 182
 pleural mesothelioma, method: 181
 pleural mesothelioma induction, rat: 183
- ASCORBIC ACID
 effect on tryptophan metabolite bladder carcinogenesis, mouse: 239
- AZOBENZENE, 4-DIMETHYLAMINO-
 and derivatives, hepatoma, DNA synthesis and cortisone-induced tryptophan oxidase, rat: 197
 hepatoma
 effect of
 liver parasites, rat: 198
 reserpine or yohimbine, rat: 206
 interaction with dimethylnitrosamine, rat: 192
- AZOBENZENE, 4-DIMETHYLAMINO- (Contd.)
 membrane-associated tumor-specific antigen, rat: 203
- AZOBENZENE, 3'-METHYL-4-DIMETHYLAMINO-
 hepatoma, guinea pig: 199
- AZO DYES
 effect on liver RNA, rat: 201
- BACTERIA
 carcinogen production, review: 162,163
- BENZANTHRACENE, 7,12-DIMETHYL-
 adrenal necrosis, rat: 214
 metopirone and Su-4885 metabolism: 209
 effect on
 LDH isoenzymes, human fibroblasts: 211
 ovarian gonadotropin response, mouse or rat: 216
 leukemia, age factors, mouse: 220
 lymphoma, effect of copper sulfate, mouse: 210
 mammary tumors
 age and sex factors, rat: 212
 effect of copper sulfate, mouse: 210
 hormone effects, rat: 219
 ovary tumors (mouse): 217
 effect of copper sulfate: 210
 metabolic inhibitors: 218
 respiratory tumors, hamster: 207
 sarcoma, s.c. graft of gastric cyst, mouse: 215
 skin tumors, mouse: 208,237
 thyroiditis, rat: 213
- BENZANTHRACENE, 7-HYDROXYMETHYL-12-METHYL-
 adrenal necrosis, rat: 214
- 3,4-BENZOPYRENE
 air pollution, coke plant, USSR: 255
 brain tumors, rat: 234
 effect on liver xoxazolamine hydrolase, hamster or rat: 180
 g.i. tumors, rat: 241
 metabolism, effect of dust or polycyclic aromatic hydrocarbons, rat liver enzymes: 205
 s.c. tumors, effect of adenovirus type 12, hamster: 303
- BLADDER CARCINOGENESIS
 dibutyl nitrosamine, enzymes, rat: 244
 tryptophan metabolites, effect of ascorbic acid, mouse: 239
- BLADDER NEOPLASMS
 malignant or preinvasive, karyotype: 342
- BONE DISEASES
 fibrous dysplasia, malignant transformation: 339
- BONE NEOPLASMS
 sarcoma, malignant transformation of fibrous dysplasia: 339
- BRAIN NEOPLASMS
 induction
 benzpyrene, rat: 234
 methylcholanthrene, rat: 234
 methylnitrosourea, rabbit: 242,253,254
 simian adenovirus-induced, virus recovery, hamster: 305

SUBJECT INDEX

- BREAST NEOPLASMS (See Mammary neoplasms, human)
- CADMIUM
 - s.c. sarcoma, enzymes, rat: 235
- CARCINOGENS (CHEMICAL)
 - bacterial or fungal, occurrence, review: 162,163
 - foods, analysis, review: 161
- CELL GROWTH KINETICS
 - glucose and lactate metabolism, high- and low-tumor-producing mouse cell clones: 345, 347
 - goitrogen-stimulated thyroid, rat: 333
 - mitotic cycle, Sendai virus-infected hamster embryo cells: 317
 - preinvasive or malignant tumors, karyotype: 342
- CERVIX UTERI NEOPLASMS
 - preinvasive or malignant, growth rate and karyotype: 342
- CHROMOSOMES
 - EB virus-infected human embryo cells: 297
 - Harvey sarcoma virus-transformed mouse or rat cells: 280
 - human leukemic cells *in vitro* and hamster transplants: 320
 - marker, ultrastructure, Burkitt lymphoma, child: 341
 - methylcholanthrene tumors, hamster: 221
 - Sendai virus-infected hamster embryo cells: 317
 - sex, relationship to trophoblastic proliferation, hydatidiform mole: 331
 - transforming mouse embryo cells, effect of culture medium: 346
 - urethan lymphoma, mouse: 238
- COLON NEOPLASMS
 - familial polyposis with malignant transformation: 336
- COPPER SULFATE
 - effect on dimethylbenzanthracene tumors, mouse: 210
- CORPUS UTERI NEOPLASMS
 - hydatidiform mole, histology, chromatin-positive or -negative tumors: 331
 - radiation-induced ichthyosis uteri: 171
- ROTON OIL PHORBOL ESTERS
 - skin tumor promotion, mechanism, mouse: 208
- YCAD SEEDS
 - toxicity, chick: 240
- YCASIN
 - kidney tumors, tissue culture characteristics, rat: 258
- DIET (See also under Foods)
 - high-fat, hepatoma, mouse: 250
 - lipotrope-deficient, effect on aflatoxin hepatocarcinogenesis, rat: 188
- DISTRIBUTION
 - dimethylnitrosamine, subcellular, mouse liver: 200
- ES AND STAINS
 - acridine orange, skin tumors, mouse: 237
- EB VIRUS (See under Virus, herpes-type)
- ENDOCRINE ABLATION
 - hypophysectomy, effect on aflatoxin liver tumor, rat: 185
- ENVIRONMENTAL FACTORS (See also specific terms, such as Air pollution, Foods and Occupational diseases)
 - nasopharynx cancer, South Vietnam: 330
 - nitrosamines, foods, review: 164
- ENZYMES
 - cadmium-induced s.c. sarcoma, rat: 235
 - cortisone-induced tryptophan oxidase, dimethylaminoazobenzene hepatoma, rat: 197
 - dibutylnitrosamine bladder tumors, rat: 244
 - diethylnitrosamine hepatoma, rat: 195
 - glutamic-oxaloacetic transaminase, isozymes, serum, human cancer: 344
 - lactate dehydrogenase isozymes, effect of dimethylbenzanthracene, human fibroblasts: 211
 - methylnitrosourea-induced brain tumors, rabbit: 242,254
 - polynucleotide ligase, SV40- or polyoma virus-infected cells: 318
 - RNase and its inhibitor, liver and spleen, ascites mouse leukemia: 343
 - zoxazolamine hydrolase, effect of benzpyrene or tobacco smoke, hamster or rat liver: 180
- EPIDEMIOLOGY
 - all tumors
 - children vaccinated with SV40-containing polio vaccine, U.S.: 316
 - Colombia (Cartagena): 329
 - France: 328
 - Italy, high-mortality rate area (Spoleto): 326
 - breast cancer: 335
 - lung cancer
 - exposure to solid fuels, international: 179
 - Italy, smoking: 325
 - (Treviso): 327
 - smoking, international: 179
 - review (book): 166
 - solid fuel exposure, international: 179
 - nasopharynx cancer, South Vietnam, environmental and genetic factors: 330
 - non-malignant respiratory disease, tobacco processing workers, Poland: 172
 - phagedenic ulcer with malignant transformation, Senegal: 332
 - second primary tumor incidence, women with salivary gland tumors: 338
 - serum antibodies
 - EB virus, Japan (Akita Prefecture): 296
 - SV40, Rous sarcoma virus and adenovirus-12, human cancer, Japan: 304
- ESOPHAGUS NEOPLASMS
 - induction
 - dibutylnitrosamine, mouse: 248
 - nitrosomethylaniline, rat: 231
- ESTRADIOL
 - mammary hyperplastic nodule induction, effect of mammary tumor or nodule-inducing virus, mouse: 286

ETHIONINE

effect on dimethylbenzanthracene ovarian tumors, mouse: 218

ETHIONINE, DL-

effect on liver RNA, rat: 201

FATS (See also Lipids and Oils, edible)

dietary, hepatoma, mouse: 250
heated, s.c. or g.i. tumors, rat: 241

FOODS (See also under Diet)

carcinogen content, analysis, review: 161
heated fats and oils, s.c. or g.i. tumors, rat: 241
nitrosamine content, review: 164

FUNGI

Candida albicans or Saccharomyces cerevisiae,
polyoma virus propagation: 322
carcinogen production, review: 162,163

GANGLIONEUROBLASTOMA

ultrastructure and catecholamine production,
child: 350

GASTROINTESTINAL CARCINOGENESIS

aflatoxin, hamster: 187
benzpyrene, rat: 241
dibutyl nitrosamine, mouse: 248
diethylnitrosamine, effect of phenobarbital
or anesthetics, mouse: 236
heated edible fats and oils, rat: 241
radiation, mouse: 167

GENETICS, ANIMAL

high-fat diet hepatoma, mouse: 250
mammary tumor pathology, NZB mice: 291

GENETICS, HUMAN

familial colon polyposis with malignant transformation: 336

GENETICS, POPULATION

cancer mortality, isolated community, Italy
(Spoleto): 326
nasopharynx cancer, South Vietnam: 330

GENITAL NEOPLASMS, MALE OR FEMALE

malignant or preinvasive, karyotype: 342

HEMATOPOIESIS

platelets, Rauscher virus leukemia, mouse: 261

HODGKIN'S DISEASE (See under Lymphoma, malignant, human)

HORMONES

effect on
dimethylbenzanthracene mammary tumor
calcification, rat: 219
DNA, virus-induced hyperplastic alveolar
mammary nodules, mouse: 292
gonadotropins, ovarian response, effect of
dimethylbenzanthracene, mouse or rat: 216

HYDRAZINE DERIVATIVES

lung tumors, mouse: 252

HYDROCARBONS

carcinogenic or non-carcinogenic, binding to
DNA and RNA, normal cells: 232
halogenated, anesthetics, effect on diethyl-
nitrosamine carcinogenesis, mouse: 236

HYDROCARBONS, POLYCYCLIC AROMATIC

effect on benzpyrene metabolism, rat liver
microsomes: 205
mechanism of action, review: 165

IMMUNITY

cellular

EB virus, properties: 300
Graffi leukemia virus-induced sarcoma,
mouse: 271
polyoma-transformed hamster cell line
variants: 312
serum-mediated inhibition, Shope papilloma
or carcinoma, rabbit: 308
SV40-transformed hamster cells (TSV5CL2):
313

group-specific tumor antigens

Bratislava-77 (avian myeloblastosis) virus-
induced rat or bird tumors: 284
Rous virus-induced rat tumors: 284

host

Graffi virus leukemia, mouse: 263
Harvey sarcoma virus immunization against
Moloney leukemia virus, mouse: 279
leukemia virus-induced immunosuppression,
mouse: 262
serum antibodies, JM avian leukosis virus-
infected chickens: 319
tumors induced by SV40-transformed mouse
kidney cells: 315
virus-induced mammary tumors, mouse: 288
neonatal vaccination with SV40-containing
polio vaccine, cancer incidence: 316
serum EB virus antibodies, Japan (Akita
Prefecture): 296
species-specific membrane antigen sites and
virus-determined antigen receptors, EB
virus, properties: 300
tumor-specific

membrane-associated antigens, dimethyl-
aminoazobenzene hepatoma, rat: 203
virus-induced mouse mammary tumors: 285,288
viral antigens, Graffi leukemia virus-induced
sarcoma, mouse: 271

IMMUNITY DISORDERS

rheumatoid arthritis, lymph node follicular
hyperplasia: 339
systemic lupus erythematosus, malignant
transformation (acute leukemia): 337

INTESTINE, LARGE, NEOPLASMS

malignant or preinvasive, karyotype: 342

IRON DEXTRAN

s.c. sarcoma, rat: 233

ISOENZYMES

glutamic-oxaloacetic transaminase, serum,
human cancer: 344
effect of dimethylbenzanthracene, human
fibroblasts: 211

ISONICOTINIC ACID HYDRAZIDE

lung tumors, mouse: 252

ISOTHIOCYANATE, α -NAPHTHYL-

effect on liver RNA, rat: 201

KIDNEY CARCINOGENESIS

aflatoxin, hamster: 187

- KIDNEY CARCINOGENESIS (Contd.)
 cycasin, tissue culture characteristics, rat: 258
 dimethylnitrosamine, rat: 243
- KIDNEY NEOPLASMS
 spontaneous, virus-like particles, morphology, BALB/cf/Cd mice: 307
- LARYNX
 pathology, smokers: 178
- LEUKEMIA, EXPERIMENTAL (See also Virus, leukemia/lymphoma)
 C-1498 or SN-36 (mouse), RNase and its inhibitor, liver and spleen: 343
 virus-containing chloroma (mouse) properties: 264
- LEUKEMIA, HUMAN
 acute myeloid
 cell lines with EB virus: 298,299
 malignant transformation of systemic lupus erythematosus: 337
 cells, karyotype, *in vitro* and in hamster: 320
 culture fluid-transformed embryonic cell line (THE-3), cross-reactivity with Burkitt lymphoma sera: 302
- LEUKEMIOGENESIS, EXPERIMENTAL
 3-acetaminophenanthrene, rat: 246
 dimethylbenzanthracene
 age factors, rat or mouse: 212,220
 effect of copper sulfate, mouse: 210
 sex factors, rat: 212
 methylcholanthrene, skin nucleic acids, mouse: 225
 urethan, tumor karyotype, mouse: 238
- LIPIDS (See also under Fats and Oils, edible)
 analysis, SV40-transformed human cell line (WI-38VA13A): 314
- LIPOTROPES
 deficiency, effect on aflatoxin hepatocarcinogenesis, rat: 188
- LIVER
 aflatoxin metabolism, rat: 184
 cholesterol synthesis, effect of aflatoxin, rat: 186
 microsomal benzpyrene metabolism, effect of other polycyclic aromatic hydrocarbons, rat: 205
 polysomes, effect of aflatoxin, rat: 190
 regeneration, effect of diethylnitrosamine, rat: 204
 RNA, effect of hepatocarcinogens, rat: 201
 RNase and RNase inhibitor, leukemic mouse: 343
 subcellular fractions, dimethylnitrosamine uptake, mouse: 200
 toxicity, aflatoxin, chick embryo: 257
 cycad seeds, chick: 240
 zoxazolamine hydrolase, effect of carcinogens, hamster or rat: 180
- LIVER CARCINOGENESIS (Contd.)
 diethylnitrosamine
 cytoplasmic protein composition, rat: 193
 effect of phenobarbital or anesthetics, mouse: 236
 guinea pig: 191
 histochemical changes, rat: 195
 ribosomal proteins, rat: 194
 specific gravity of cells, rat: 196
 dimethylaminoazobenzene
 DNA synthesis and cortisone-induced tryptophan oxidase, rat: 197
 effect of liver parasites, rat: 198
 reserpine or yohimbine, rat: 206
 interaction with dimethylnitrosamine, rat: 192
 transplantable tumor (D23), membrane-associated tumor-specific antigens, rat: 203
 dimethylnitrosamine (rat): 247
 interaction with dimethylaminoazobenzene: 192
 high-fat diet, mouse: 250
 methyl dimethylaminoazobenzene, guinea pig: 199
 nitrosomorpholine, ribosomal proteins, rat: 194
 thioacetamide, ribosomal proteins, rat: 194
- LIVER NEOPLASMS
 dimethylaminoazobenzene rat hepatoma (D23), membrane-associated tumor-specific antigens: 203
 function, ^{198}Au detection method, mouse: 169
 serum zinc levels, South Africa (Bantu): 202
- LUNG CARCINOGENESIS
 dibutylnitrosamine, mouse: 248
 diethylnitrosamine, effect of phenobarbital or anesthetics, mouse: 236
 hydrazines and related compounds, mouse: 252
 2-nitroquinoline, mouse: 251
- LUNG DISEASES
 asbestosis, asbestos detection: 182
- LUNG NEOPLASMS
 epidemiology
 Italy, smoking: 325
 (Treviso): 327
 smoking, international: 179
 review (book): 166
 solid fuel exposure, international: 179
- LUPUS ERYTHEMATOSUS, SYSTEMIC (See under Immunity disorders)
- LYMPHOMA, MALIGNANT, EXPERIMENTAL
 dog mast cell tumor, virus-like particles: 282
- LYMPHOMA, MALIGNANT, HUMAN
 Burkitt, marker chromosome ultrastructure, child: 341
 Hodgkin's disease, cell lines, properties: 267,299
- LYMPH NODES
 follicular hyperplasia, rheumatoid arthritis: 340
- MALIGNANT TRANSFORMATION
 familial polyposis to colon cancer: 336

MALIGNANT TRANSFORMATION (Contd.)

- fibrous dysplasia to sarcoma of bone: 339
- mouse embryo cells, karyotype, effect of culture medium: 346
- prostate cell lines: 348
 - methylcholanthrene-induced: 226
- phagedenic ulcer to carcinoma, epidemiology, Senegal: 332
- systemic lupus erythematosus to acute leukemia: 337

MAMMARY CARCINOGENESIS, EXPERIMENTAL (See also Virus, mammary tumor)

- aminophenanthrene derivatives, rat: 246
- chemical or radiation, method, mouse: 289
- dimethylbenzanthracene
 - age and sex factors, rat: 212
 - effect of copper sulfate, mouse: 210
 - hormone effects, rat: 219
- estradiol + pituitary graft, hyperplastic nodules, effect of nodule-inducing or mammary tumor virus, mouse: 286
- viral or chemical, epithelial-mesenchymal junction ultrastructure, mouse: 349

MAMMARY NEOPLASMS, EXPERIMENTAL

- mammary tumor virus immunity, mouse: 285
- pathology, NZB mice: 291

MAMMARY NEOPLASMS, HUMAN

- epidemiology and endocrinology: 335
- incidence, women with salivary gland tumors: 338
- malignant or preinvasive, karyotype: 342
- virus-like particles: 293,294,295

MAST CELL TUMOR, CANINE (See under Lymphoma, malignant, experimental)

METABOLISM (glycolysis and respiration)

- high- and low-tumor-producing mouse cell clones: 345,347

3-METHYLCHOLANTHRENE

- brain tumors, rat: 234
- effect on mouse prostate cell line: 226
- lymphoma, skin nucleic acids, mouse: 225
- mammary tumors, ultrastructure, epithelial-mesenchymal junction, mouse: 349
- skin tumors
 - effect of antitumor antibiotic, mouse: 256
 - relationship to collagen properties, mouse: 223,224
- transplanted tumors, karyotype, hamster: 221

NASOPHARYNX NEOPLASMS

- epidemiology, South Vietnam, environmental and genetic factors: 330

NEOPLASMS, EXPERIMENTAL

- Dr-Sd melanoma (fish), effect of amino acids on DNA: 334
- high-tumor-producing mouse clone (NCTC-2472), glucose and lactate metabolism: 345,347
- low-tumor-producing mouse clones (NCTC 2445 or 2555), glucose and lactate metabolism: 345,347
- polyoma virus-induced, rat, standardization: 311
- Sarcoma #37 (mouse), virus-like particles, properties: 283

NEOPLASMS, HUMAN

- epidemiology
 - Colombia (Cartagena): 329
 - France: 328
 - Italy, high-mortality rate area (Spoleto): 326
- second primary tumor incidence, women with salivary gland cancer: 338
- serum glutamic-oxaloacetic transaminase isoenzymes: 344

2-NITROQUINOLINE

- lung tumors, mouse: 251

4-NITROQUINOLINE 1-OXIDE

- chemistry, free radical reactions: 259
- interaction with
 - DNA and RNA, mechanism: 227,230
 - proteins and amino acids, mechanism: 228
- skin tumors, effect of nitroquinoline oxide derivatives, mouse: 229

4-NITROQUINOLINE 1-OXIDE, DERIVATIVES

- subeffective doses, mechanism of detection, mouse skin: 229

NITROSAMINES

- environmental, review: 164

NITROSAMINE, DIBUTYL-

- bladder tumors, enzymes, rat: 244
- respiratory and g.i. tumors, mouse: 248

NITROSAMINE, DIETHYL-

- effect on liver regeneration, rat: 204
- hepatoma
 - analysis of cytoplasmic proteins, rat: 193
 - effect of anesthetics, mouse: 236
- guinea pig: 191
- function, detection method, mouse: 169
- histochemical changes, rat: 195
- ribosomal proteins, rat: 194
- specific gravity of cells, rat: 196
- lung or g.i. tumors, effect of anesthetics, mouse: 236

NITROSAMINE, DIMETHYL-

- hepatoma, rat: 247
 - interaction with dimethylaminoazobenzene: 192
- kidney tumors, rat: 243
- uptake, subcellular fractions, mouse liver: 200

NITROSAMINE, DIMETHYLTHIO-

- toxicity, rat: 247

N-NITROSOANILINE, N-METHYL-

- esophagus tumors, rat: 231

N-NITROSOMORPHOLINE

- hepatoma, ribosomal proteins, rat: 194

N-NITROSOUREA, N-ETHYL-

- dysontogenic skin tumors, fetal pig: 249

N-NITROSOUREA, N-METHYL-

- brain tumors, rabbit: 242,253,254
- spinal cord tumors, rabbit: 253

NUCLEIC ACIDS, DNA

- binding, carcinogenic or non-carcinogenic hydrocarbons, normal cells: 232
- dimethylaminoazobenzene hepatoma, rat: 197
- effect of
 - amino acids, fish melanoma explants: 334
 - carcinogenic or non-carcinogenic quinoline oxides, normal cells: 230

SUBJECT INDEX

- NUCLEIC ACIDS, DNA (Contd.)
 diethylnitrosamine, regenerating rat liver: 204
 hormone effects, virus-induced hyperplastic alveolar mammary nodules, mouse: 292
 interaction with nitroquinoline oxide, mechanism: 227
 Rous virus-infected chick embryo cells: 276
 skin, mouse with methylcholanthrene lymphoma: 225
- NUCLEIC ACIDS, RNA
 binding, carcinogenic or non-carcinogenic hydrocarbons, normal cells: 232
 effect of
 carcinogenic or non-carcinogenic quinoline oxides, normal cells: 230
 hepatocarcinogens, rat liver: 201
 Rous virus-infected chick embryo cells: 276
 skin, mouse with methylcholanthrene lymphoma: 225
- OCCUPATIONAL DISEASES
 solid fuel exposure, lung cancer, international: 179
 tobacco processing, respiratory diseases, Poland: 172
- OILS, EDIBLE
 heated, s.c. or g.i. tumors, rat: 241
- OVARY
 gonadotropin response, effect of dimethylbenzanthracene, mouse or rat: 216
- OVARY NEOPLASMS
 induction
 dimethylbenzanthracene (mouse): 217
 effect of copper sulfate: 210
 metabolic inhibitors: 218
 malignant or preinvasive, karyotype: 342
- PARASITIC DISEASES
Cysticercus, effect on dimethylaminoazobenzene hepatoma, rat: 198
- BENZANTHRENE, 3-ACETAMINO-
 leukemia, rat: 246
- BENZANTHRENE, AMINO-, DERIVATIVES
 mammary tumors, rat: 246
- PHENOBARBITAL
 effect on diethylnitrosamine carcinogenesis, mouse: 236
- PHORBOL ESTERS (See Croton oil phorbol esters)
- PLANT EXTRACTS
 reserpine or yohimbine, effect on dimethylaminoazobenzene hepatoma, rat: 206
- EURA NEOPLASMS
 mesothelioma
 asbestos detection, method: 181
 induction, rat: 183
- EGNANCY
 transplacental skin carcinogenesis, ethylnitrosourea, swine: 249
- OSTATE
 mouse, cell lines, malignant transformation: 226,348
- PROTEINS
 cytoplasmic or ribosomal, induced hepatoma, rat: 193,194
- PROTEINS (Contd.)
 interaction with nitroquinoline oxide, mechanism: 228
- QUINOLINE, 4-AMINO-, 1-OXIDE
 effect on DNA and RNA, normal cells: 230
- QUINOLINE, 4-HYDROXYAMINO-, 1-OXIDE
 effect on DNA and RNA, normal cells: 230
- RADIATION CARCINOGENESIS
 skin, mouse: 168
 stomach, mouse: 167
- RADIATION EFFECTS
 tumor growth from high- or low-tumor-producing cell clones, mouse: 347
- RESPIRATORY CARCINOGENESIS
 dimethylbenzanthracene, hamster: 207
- RESPIRATORY TRACT
 dye retention, effect of smoking, human: 173
 non-malignant diseases, tobacco processing workers, Poland: 172
- SALIVARY GLAND NEOPLASMS
 incidence of breast cancer and other second primary tumors: 338
- SCAR TISSUE
 phagedenic ulcer, malignant transformation, Senegal: 332
- SEX CHROMOSOMES
 relationship to trophoblastic proliferation, hydatidiform mole: 331
- SEX FACTORS
 dimethylbenzanthracene carcinogenesis, rat: 212
- SKIN
 collagen, effect of methylcholanthrene, mouse: 222,223,224
 s.c. graft of stomach wall, sarcoma induction by dimethylbenzanthracene, mouse: 215
- SKIN CARCINOGENESIS
 acridine orange, mouse: 237
 dimethylbenzanthracene
 age and sex factors, rat: 212
 mouse: 237
 + phorbol esters, mechanism, mouse: 208
 ethylnitrosourea, fetal pig: 249
 methylcholanthrene
 effect of antitumor antibiotic, mouse: 256
 relation to collagen properties, mouse: 222,223,224
 transplanted tumors, karyotype, hamster: 221
 nitroquinoline oxide, mouse: 229
 radiation, mouse: 168
 s.c. tumors
 cadmium, enzymes, rat: 235
 heated edible fats and oils, rat: 241
 iron dextran, rat: 233
 tobacco smoke, mouse: 174,175,176,177
- SKIN NEOPLASMS
 malignant or preinvasive, karyotype: 342
 melanoma, effect of amino acids on DNA, fish: 334

- SKIN NEOPLASMS (Contd.)
 phagedenic ulcer with malignant transformation,
 epidemiology, Senegal: 332
 photochemical repair defect, human: 170
- SPINAL CORD NEOPLASMS
 induction, methylnitrosourea, rabbit: 253
- STILBENE, 4-ACETAMIDO-
 metabolism, rat: 245
- STILBENE, N-HYDROXY-4-ACETAMIDO-
 metabolism, rat: 245
- STOMACH
 s.c. graft, sarcoma induction by dimethyl-
 benzanthracene, mouse: 215
- STOMACH NEOPLASMS
 cell lines (MC-8 or MC-12) with EB virus,
 human: 299
 induction
 dibutyl nitrosamine, mouse: 248
 radiation, mouse: 167
- SV40 (See under Virus, papova)
- THYROID
 dimethylbenzanthracene thyroiditis, rat: 213
 growth curve, effect of goitrogen, rat: 333
- TOBACCO
 occupational exposure, respiratory diseases,
 Poland: 172
- TOBACCO SMOKE
 effect on liver xoxazolamine hydrolase,
 hamster and rat: 180
 skin tumors, mouse: 174,175,176,177
- TOBACCO SMOKING
 effect on
 dye retention, human respiratory tract:
 173
 larynx, human: 178
 photochemical repair, human oral mucosa:
 170
 health hazard, review (book): 166
 lung cancer
 international: 179
 Italy: 325
- TOXICITY
 aflatoxin, liver, chick embryo: 257
 dimethylthionitrosamine, rat: 247
- TRYPTOPHAN METABOLITES
 bladder tumors, effect of ascorbic acid,
 mouse: 239
- URETHAN
 lymphoma, karyotype, mouse: 238
- UTERUS NEOPLASMS (See Corpus uteri neoplasms)
- VIRUS
 fish epidermal hyperplasia, properties:
 323,324
 plant tumor, multiplication and cytopathology,
 insect: 321
 Sendai, effect on chromosomes and mitosis,
 hamster embryo cells: 317
- VIRUS, ADENO-
 SA7 (simian), brain tumors, hamster: 305
 Type 5 (Prague strain)
 growth, human cancer (HeLa) cells: 306
- VIRUS, ADENO- (Contd.)
 Type 7 (Iasi strain)
 growth, human cancer (HeLa) cells: 306
 Type 12
 effect on benzpyrene carcinogenesis,
 hamster: 303
 serum antibodies, human cancer: 304
- VIRUS, HERPES-TYPE
 Epstein-Barr (human; Burkitt lymphoma)
 cell lines, membrane immunofluorescence:
 301
 human embryo cells, karyotype and virus
 replication: 297
 isolation, human leukemia, lymphoma or solid
 tumor cell lines: 298,299
 reaction with leukemia culture fluid-
 transformed human embryonic cells: 302
 serum antibodies, incidence, Japan (Akita
 Prefecture): 296
 transformation, human embryo cells: 298
 virus-determined antigen receptors and
 species-specific membrane antigen sites,
 properties: 300
- VIRUS, LEUKEMIA/LYMPHOMA
 attempted isolation, Hodgkin's disease cell
 line (AICHI-4): 267
 Bratislava-77 (avian myeloblastosis)
 group-specific antigens, rat, chick or
 duckling tumors: 284
 dog mast cell tumor, morphology: 282
 Friend (mouse)
 effect of acetylenic carbamate, mouse: 265
 inhibition, extract from Rauscher virus-
 infected cell line: 266
 isolation, mouse chloroma: 264
 non-leukemogenic strain, properties: 268
 Graffi (mouse)
 pathology and immunology *in vivo*: 263
 sarcoma, viral and cellular antigens: 271
 JM (avian leukosis)
 serum antibodies, chicken: 319
 Moloney (mouse)
 immunization by Harvey sarcoma virus, mouse:
 279
 mouse
 particles resembling, spontaneous kidney
 tumor, BALB/cf/Cd mice: 307
 properties and pathogenicity, chloroma:
 264
 Rauscher (mouse)
 effect of antitumor agent *in vitro*: 272
 enhancement of Moloney virus sarcoma
 in vivo: 270
 immunosuppressive effect, mouse: 262
 infected spleen, cell line (JLSV-5),
 extract with anti-Friend virus
 properties: 266
 infection, effect on platelets, mouse: 261
 transformed cell lines (OUMS-1 and OUMS-2),
 properties: 260
- VIRUS, MAMMARY TUMOR
 human
 morphology, breast cancer: 293,294,295
 mouse
 development of Type A particles: 287

SUBJECT INDEX

VIRUS, MAMMARY TUMOR (Contd.)

- effect on hormone-induced hyperplastic alveolar nodule outgrowth cell line (D1): 286
- hyperplastic alveolar nodules, hormonal control of DNA synthesis: 292
- isolation and properties: 290
- particles resembling, spontaneous kidney tumor, BALB/cf/Cd mice: 307
- tumor antigen changes, syngeneic hosts: 288
- tumor-specific immunity: 285
- tumor ultrastructure, epithelial-mesenchymal junction: 349
- nodule-inducing virus (mouse)
- effect on hormone-induced hyperplastic alveolar nodule cell line (D1): 286

RUS, PAPOVA (papilloma-polyoma-vacuolating)

- bovine papilloma
- serum precipitin response, cattle: 309
- canine papilloma
- structure: 310
- Graffi BB/T2 polyoma
- rat tumors, standardization: 311
- polyoma
- infected cells, polynucleotide ligase: 318
- propagation in fungi: 322
- rat tumors, standardization: 311
- transformed hamster cells, cell membrane properties: 312
- Shope papilloma (rabbit)
- cellular immunity and serum-mediated inhibition of immunity: 308
- SV40
- infected cells, polynucleotide ligase: 318
- polio vaccine, neonatal vaccination, cancer incidence in childhood: 316
- serum antibodies, human cancer: 304
- transformed cells

VIRUS, PAPOVA (papilloma-polyoma-vacuolating)(Contd.)

- hamster (TSV5CL2), new antigens: 313
- human (WI-38VA13A), lipid composition: 314
- mouse kidney (mKS strains), properties of mouse tumors: 315
- VIRUS, SARCOMA
- Harvey (mouse)
- immunization against Moloney leukemia virus, mouse: 279
- transformed mouse or rat cells, karyotype: 280
- tumor pathology, mouse: 281
- isolation and properties, Sarcoma #37 (mouse): 283
- Moloney (mouse)
- effect of antitumor agent in vitro: 272
- enhancement, Rauscher virus, in vivo: 270
- interference, non-leukemogenic Friend virus strain: 268
- tumor pathology, mouse: 281
- RAV-1 (avian)
- growth rate, infected cells: 269
- Rous (chicken)
- Carr-Zilber strain, mouse-adapted, properties: 277,278
- effect on nucleic acids and growth, chick embryo cells: 276
- growth rate of infected cells: 269
- hamster tumors, pathology: 273
- mouse-adapted strain, hamster tumor induction: 277
- production, mixed mammalian-chick embryo cell cultures: 274
- rat tumors, group-specific tumor antigens: 284
- serum antibodies, human cancer: 304
- transformation, monkey kidney cells: 275
- ZINC
- serum, hepatoma, South Africa (Bantus): 202

U.S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

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MARCH 1970

Abstract Nos. 351-556



CARCINOGENESIS ABSTRACTS

National Cancer Institute

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE • National Institutes of Health

CARCINOGENESIS ABSTRACTS

Volume 8, Number 3
March, 1970

Abstract Numbers
351-556

CONTENTS

	<u>Page</u>
Review	73
Physical Carcinogenesis	74
Chemical Carcinogenesis	75
Viral Carcinogenesis	91
Epidemiology and Biometry	109
Miscellaneous	115
Author Index	i
Subject Index	iv

Prepared by Scientific Literature Corporation
Philadelphia, Pennsylvania 19103

S. Sim Kessler, Director

Editorial Advisors: Leila Diamond, Ph.D.
Wistar Institute, Philadelphia

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Persuant to a Contract with the Public Health Service
U.S. Department of Health, Education and Welfare
PH43-70-2036

Use of funds for printing this publication approved
by the Director of the Bureau of the Budget on July 25, 1967.

FOREWORD

The National Cancer Institute, in response to Congressional interest and desire for a national program of cooperative research in cancer, is establishing a means whereby information in the field of carcinogenesis will be coordinated and made available. The information to be included will be obtained from the National Cancer Institute, other governmental agencies, and non-governmental research institutions.

The issuing of Carcinogenesis Abstracts under the auspices of the National Cancer Institute will provide a central source for current abstracting of the carcinogenesis literature being published throughout the world. This will help facilitate an integrated and cooperative program of investigation in this area. The growing number of publications in the area of carcinogenesis makes imperative the availability of an appropriate abstracting service so that investigators may be apprised of progress with a minimum of delay. It is our desire to provide the investigator with a readily systematized compilation of the published work.

Carcinogenesis Abstracts will be published monthly and will include abstracts from the most recently published literature.

Inquiries may be addressed as follows:

Carcinogenesis Abstracts
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NOTE

Journal names are abbreviated according to the list of abbreviations used by Index Medicus. If the journal is not covered by Index Medicus, then the abbreviations (with some modifications) found in World Medical Periodicals, 3rd Edition, are used.

ABBREVIATIONS USED IN ABSTRACTS

admin.	administered, administration	mg	milligram(s)
av.	average	min.	minute(s)
C	curie(s)	ml	milliliter(s)
mC	millicurie(s)	mm	millimeter(s)
μC	microcurie(s)	mo.	month(s)
cm	centimeter(s)	MTD	maximum tolerated dose
conc.	concentration	NIH	National Institutes of Health, USA
cpm	counts per minute	p.o.	orally
DNA	deoxyribonucleic acid	QO ₂	oxygen quotient
DNase	deoxyribonuclease	PFU	plaque forming unit
e.g.	for example	ppm	parts per million
FFU	focus forming unit	pt.(s)	patient(s)
g.i.	gastrointestinal	RBC	red blood cells (erythrocytes)
g	gram(s)	RES	reticuloendothelial system
μg	microgram(s)	resp.	respectively
Hb	hemoglobin	RNA	ribonucleic acid
i.a.	intra-arterial	RNase	ribonuclease
ID ₅₀	median infectious dose	soln.	solution
inj.	injected, injection(s)	s.c.	subcutaneous
inoc.	inoculated, inoculation(s)	TCID	tissue culture infectious dose
i.p.	intraperitoneal	x	times (e.g. x 3/wk.)
I.U.	international unit(s)	U	unit
i.v.	intravenous	UV	ultraviolet
g	kilogram(s)	vol.	volume
D ₅₀	median lethal dose	VA	Veterans Administration
M	molar, mole(s)	wt.	weight
M	millimole(s)	WBC	white blood cells (leukocytes) or white blood cell count
M	micromole(s)		
max.	maximum	yr.	year(s)

LANGUAGE ABBREVIATIONS

f.	Afrikaans	E.	English	Hun.	Hungarian	Lith.	Lithuanian	Ser.	Serbo-Croatian
r.	Arabic	Eston.	Estonian	lc.	Icelandic	Maced.	Macedonian	Sl.	Slovene
bl.	Bulgarian	Fin.	Finnish	In.	Indonesian	Nor.	Norwegian	Sp.	Spanish
h.	Chinese	Fr.	French	It.	Italian	Pol.	Polish	Sw.	Swedish
z.	Czech	Ger.	German	Jap.	Japanese	Por.	Portuguese	Th.	Thai
an.	Danish	Gr.	Greek	Kor.	Korean	Rum.	Rumanian	Uk.	Ukrainian
ut.	Dutch	Heb.	Hebrew	Latv.	Latvian	Rus.	Russian	Viet.	Vietnamese

0-351 MICROINVASION OF EPIDERMIS CAUSED BY SUBSTITUTED ANISOLES. (E.) Grasso, P. Brit. Indust. Biol. Res. Ass., Surrey, England) and C. C. Rostron. Nature (London) 225(5228): 188-189, 1970. (13 references)

It is suggested that the epidermal pseudopods induced by prolonged applications of butylated hydroxyanisole and related compounds (3- or 4-hydroxyanisole) are merely the ultrastructural counterpart of the initial proliferative activity, observed by light microscopy, induced by applications of either a carcinogen or a simple irritant, and may be reversible.

0-352 CHEMICAL CARCINOGENESIS. (E.) Burrows, T. W. (Microbiol. Res. Estab., Salisbury, England). Brit. J. Cancer 23(4): 751-754, 1969. (No references)

The mechanism of chemical carcinogenesis is proposed, in which a promotor, by interfering with chromosomal distribution during cell division, causes homozygosity of recessive genes mutated by an initiator.

0-353 RESONANCE TRANSFER OF EXCITATION ENERGY BETWEEN AROMATIC AMINO ACIDS AND CARCINOGENIC AROMATIC COMPOUNDS AS A POSSIBLE MECHANISM IN CARCINOGENESIS. (E.) Mizuno, K. (Nagai Pharmaceut. Co., Ltd., Tokyo), S. Hata and S. Tomioka. Gann 60(5):469-481, 1969. (10 references)

The overlap integrals J of the resonance transfers between aromatic amino acids, on the one hand, and 85 carcinogenic aromatic compounds or 7 noncarcinogenic aromatic compounds, on the other hand, were tabulated from the literature and from the authors' experiments. The J values of the carcinogenic aromatic compounds tended to cluster in a constant region and correlated with carcinogenic activity only using the aromatic amino acid tryptophan.

0-354 ANTIGENS OF VIRUS-INDUCED TUMORS. Habel, K. Pp. 229-249 in Advances in Immunology, Dixon, F. J., Jr. and H. G. Kundel (Eds.). Academic Press, New York, 1969, 333 pp. (8 references)

The properties of surface, intracellular, and structural antigens of virus-induced animal tumors are reviewed in relation to the immunologic reactivity of the host and the detection of such antigens in humans.

70-355 A CRITICAL STUDY OF SO-CALLED BURKITT'S LYMPHOMA (AN AFRICAN LYMPHOMA). (Por.) de Carvalho, A. R. L. (Cancer Clin., Recife, Brazil). Rev. Bras. Cirurg. 56(3-4):339-345, 1969. (31 references)

A review of the etiology, epidemiology, geographic distribution, histology and pathologic anatomy of Burkitt's lymphoma concludes that many reports of this disorder may have involved other disease entities (particularly, lymphosarcomas and benign lymphoreticular hyperplasia in the presence of parasitic or infectious disorders), in addition to exaggerating the frequency of its appearance due to involuntary case selection.

70-356 CANCER OF THE CERVIX. (Fr.) Merz, W. R., A. Curchod and F. Von Niederhäusern. Rev. Med. Suisse Rom. 89(6): 515-546, 1959. (46 references)

An extensive review of the diagnosis, treatment and postoperative or posttreatment course of cancers of the cervix includes report of the treatment of 293 cases at the University of Lausanne between 1959-1965, inclusive. Of these, 16.7% were incipient and 23.8%, 36.5%, 16.2% and 6.4% represented Stages I through IV, resp. None of the pts. was under 25 yr. of age. The highest frequency of occurrence was between ages 45-54 yr. A total of 133 pts. were pre- and 160 were postmenopausal; 38/293 were nulliparous, 67/293 were primiparous, 188/293 were multiparous.

70-357 TRANSMISSIBLE VENEREAL TUMORS OF DOGS. (E.) Stookey, J. L. (Armed Forces Inst. Path., Washington, D. C.). Nat. Cancer Inst. Monogr. 32:315-320, 1969. (12 references)

The gross and microscopic characteristics of the transmissible venereal tumor of the dog are described, with a discussion of evidence suggesting a viral etiology for this tumor.

See also abstract no.: 366

70-358 CLINICAL PROBLEMS OF GASTRIC STUMP CARCINOMA. (Ger.) Kutas, J. (Med. U. Pecs, Hungary), L. Póka and R. Laky. Bruns Beitr. Klin. Chir. 217(7):597-603, 1969.

Between 1939-1968 inclusive, 16 cases (all males, av. age 56.2 yr.) of gastric stump carcinoma were seen at the surgical clinic in Pecs. These constituted 0.50% of the 3205 gastric resections (for ulcer) and 1.55% of 1030 cases of gastric carcinoma seen during the same period. Four of these were seen between 1949-1958 (0.26% of 1520 resections and 0.98% of 408 gastric carcinomas) and 12 between 1959-1968 (1.90% of 629 resections and 3.44% of gastric tumors). In these pts. gastric resection (for duodenal or ventricular ulcer) was performed 4-32 yr. (av. 17.3 yr.), prior to diagnosis of stump carcinoma and comparison of incidence with number of resections performed 20 yr. previously gave a relative incidence of 0.71% for the 4 of 1948-1959 and 0.95% for the 12 of 1959-1968 indicating that gastric resection does not result in increased incidence of stump carcinoma.

70-359 CARCINOMA OF THE GASTRIC STUMP AFTER GASTRECTOMY BECAUSE OF PEPTIC ULCER. (Pol.) Bednarzewski, J. (Acad. Med., Lublin, Poland) and H. Florkiewicz. Pol. Tyg. Lek. 24(25):964-966, 1969.

Four cases of carcinoma in the remaining stomach stump are described. In a 70-yr.-old, a 53-yr.-old, a 55-yr.-old and a 60-yr.-old pt., carcinoma was discovered 7, 4, 8 and 18 yr., resp., after gastrectomy. The long time interval between gastrectomy and development of carcinoma in the gastric stump indicates that the neoplasm in these patients developed independently from the former stomach or duodenal ulcers.

70-360 CANCER DEVELOPING ON THE SCAR TISSUE OF A CAUSTIC-INDUCED ESOPHAGEAL STENOSIS DATING FROM CHILDHOOD. (Fr.) Grosdidier, J. (Marin Hosp. Surg. Clin., Nancy,

France), D. Robert, F. Watelet and R. Parietti. Sem. Hop. Paris 45(41):2512-2513, 1969.

Four yr. after gastrostomy for esophageal stenosis caused by swallowing caustic potash at the age of 16, a young woman underwent a series of 28 dilatations for renewed, severe dysphagia, then remained symptom-free for 13 yr., except for 1 brief episode at age 24, treated successfully with antispasmodics. At the end of this symptom-free period, an episode of total dysphagia yielded to another series of dilatations. Approximately 4 yr. later, severe dysphagia accompanied by spontaneous regurgitation and rapid wt. loss over a period of 3 mo. led to surgical intervention and removal of a clearly differentiated, spinocellular carcinoma arising from the old scar tissue and compressing the esophagus at the juncture of the middle and lower thirds.

70-361 PRESENCE OF AN ADDITIONAL METACENTRIC CHROMOSOME IN AKR/TIALD LEUKAEMIC CELLS. (E.) Legrand, E. (Pasteur Lab., Paris) and J. F. Duplan. Nature (London) 225(5234): 737-738, 1970.

One group of mice (AKR/TIALD substrain) was whole-body irradiated with 900 rad and then given $0.7-1.0 \times 10^7$ AKR and AKR/TIALD marrow cells. Another group received 4 weekly doses of 175 rad, and were then given marrow cells or left untreated. When signs of leukemia developed, 125 mg colchicine was given i.p. and the animal sacrificed 1.5 hr. later. Examination of thymic and marrow cells of controls, with spontaneously occurring leukemia, demonstrated a high incidence of a third metacentric chromosome in the AKR/TIALD substrain, and a comparable high frequency of extra acrocentric chromosomes among the AKR strain. No correlation was found between leukemogenesis and the incidence of a third metacentric chromosome, whereas the frequency of one or more extra acrocentric chromosomes was higher in both irradiated groups. Animals given marrow cells had chromosomal patterns which tended towards those of the donor.

CHEMICAL CARCINOGENESIS

70-362 HEPATOMA AND RENAL TUBULE ADENOMA IN RATS FED AFLATOXIN AND CYCLOPROPENOID FATTY ACIDS. (E.) Lee, D. J. (Oregon State U., Corvallis), J. H. Wales and R. O. Sinnhuber. J. Nat. Cancer Inst. 43(5):1037-1044, 1969.

Weanling male Long-Evans rats were fed diets containing a crude aflatoxin preparation (50% B₁ - 42% G₁; 0.0184-0.736 ppm = 18.4-736 ppb); some rats admin. the 3 lowest doses (0.0184-0.552 ppm) also received Sterculia foetida oil, which supplied cyclopropenoid fatty acids (CPFA; 220 ppm). During the 18-mo. experiment, 29/84 (34%) developed renal tubular adenomas, 8/84 (10%) showed malignant hepatomas (hepatocellular carcinomas), and 26/84 (31%) developed hyperplastic liver nodules. Admin. of CPFA caused a slight but significant decrease in the growth rate; the total tumor incidence was slightly higher in CPFA-treated rats (70%) than in rats admin. aflatoxin alone (59%).

70-363 CARCINOGENESIS IN RATS BY AFLATOXINS B₁, G₁, AND B₂. (E.) Butler, W. H. (Med. Res. Council Labs., Surrey, England), M. Greenblatt and W. Lijinsky. Cancer Res. 29(12):2206-2211, 1969.

Random-bred MRC rats (8-9 wk. old) were admin. purified aflatoxin B₁, B₂ or G₁ in the drinking water for 10 or 20 wk. (usually 20 µg/day). At total doses of 2 and 1 mg, aflatoxin B₁ induced liver tumors in 19/30 and 3/10 rats, resp.; kidney tumors developed in 2/30 and 0/10, resp. The same total doses of aflatoxin G₁ induced liver tumors in 3/30 and 1/10, resp., and kidney tumors in 5/30 and 0/10, resp. A higher dose of aflatoxin G₁ (60 µg/day x 20 wk., total 6 mg) induced liver and kidney tumors in 21/26 and 26, resp. No liver or kidney tumors developed in rats admin. aflatoxin B₂ for 10 wk. (total dose 1 mg). Liver tumors (nearly all were hepatocellular carcinomas) developed with equal frequency in male and female rats, but all rats developing kidney tumors were males. It is concluded that aflatoxin G₁ is carcinogenic to rats, and that its carcinogenic activity (especially for the kidney) is of the same order of magnitude as that of aflatoxin B₁.

70-364 MUTAGENIC ACTION OF AFLATOXIN B₁ ON TRANSFORMING DNA AND INHIBITION OF DNA TEMPLATE ACTIVITY IN VITRO. (E.) Maher, V. M. (Yale U. Sch. Med., New Haven, Conn.) and W. C. Summers. Nature (London) 225(5227):68-70, 1970.

In the presence of aflatoxin B₁ (AB), the transforming activity of DNA from Bacillus subtilis S9 (in the tryptophan-requiring B. subtilis strain T3) was reduced to 13% of control levels and mutations occurred with an increase in frequency of up to 23-fold. Since 35% of these

mutations were irreversible, they were presumably deletion mutation. AB altered the ability of DNA to act as a template for RNA transcription.

70-365 AFLATOXIN EFFECTS IN POULTRY. (E.) Kratzer, F. H. (U. California, Davis), D. Bandy, M. Wiley and A. N. Booth. Proc. Soc. Exp. Biol. Med. 131(4):1281-1284, 1969.

In Arbor-Acres broiler chicks fed diets containing 0.4 ppm aflatoxin (predominantly B₁, with smaller amounts of B₂, G₁ and G₂) from age 1 day-8 wk., no adverse effects and no pathological changes in the liver were detected. Aflatoxin levels of 0.4-1.6 ppm (400-1600 ppb) caused some biochemical and pathological changes. At the highest dosage, most chicks showed pathological changes in the liver, but no traces of aflatoxin were noted in the meat, liver or blood. In White Leghorn laying hens fed aflatoxin (2.7 ppm) for 48 days, pathological changes in the liver were minimal or mild. Feed intake, body wt. and egg production remained unchanged, although the hatchability of the eggs declined somewhat. No traces of aflatoxin were found in the eggs (collected in the last 34 days of the experiment) or in the meat, liver or blood of the hens.

70-366 RECENT FINDINGS CONCERNING FUNGUS CONTAMINANTS OF FOODSTUFFS. 1 - THE EFFECT OF THEIR TOXINS ON THE LIVING CELL. 2 - FACTORS FACILITATING CONTAMINATION: PROPOSED PROPHYLACTIC MEASURES. (Fr.) Monjour, L. (Org. Res. Food Nutr. African, Dakar, Senegal), J. Toury and C. Mariage. Aliment. Vie 56(10-11-12): 229-249, 1968. (126 references)

A review of mycotoxins which contaminate food-stuffs includes a brief section on the varieties of Fusarium and Cladosporium which contaminate grain, even in the polar regions, and one on luteoskyrine. Supplementing a lengthy discussion of the aflatoxins and dehydroaflatoxins (including their effects on various species, biochemistry, immunologic activities and characteristics, possible carcinogenic activity, methods of preventing contamination of foodstuffs, and methods of detoxifying those which have become contaminated), the authors report that aflatoxin was demonstrable in the hepatic cells of only 1/100 Africans who were autopsied without regard to the cause of death: a youth who had died of pneumonia.

70-367 EFFECTS OF INGESTING AFLATOXIN ON PROTEIN SYNTHESIS IN THE RAT. AN IMMUNOLOGIC STUDY. (Fr.) Monjour, L. (ORANA, Dakar, Senegal) and C. Mariage. C. R. Soc. Biol. (Paris) 163(1):274-277, 1969.

The immunoelectrophoretic activity of serum from rabbits immunized with serum from normal male Wistar Commentry rats (ASNR), was completely extinguished when a mixture of sera (SAFR) derived from rats of the same strain ingesting impure aflatoxin daily for 14 mo. was added to it in a proportion of 1 part ASNR to 0.08 parts SAFR. The extinguished immune serum no longer reacted with SAFR; however, it reacted sharply with serum derived from normal rats of the same strain, showing in the serum of rats ingesting aflatoxin the loss of 1 precipitin line which was situated in the α_1 -globulin zone. In the light of a number of previously published studies, this toxic inhibition appeared to result from a modification of the model activity of DNA (due to the disappearance of DNA from certain sites, where it was masked by the aflatoxin molecule), rather than a direct interaction of the impure aflatoxin with DNA and RNA polymerase.

70-368 MALIGNANT ETHMOID TUMORS IN WOODWORKERS.
(Fr.) Gignoux, M. and P. Bernard.
J. Med. Lyon 50(1164):731-736, 1969.

Among pts. presenting with malignant tumors of the ethmoid or ethmoid and maxillary sinuses over a period of 15 yr., 17/53 were woodworkers by occupation (all male), with 12/17 engaged in cabinet making, 3/17 in carpentry, and 1/17 (each) a cooper and a worker in a saw mill. Their mean age was 58 yr. and all of the men had been working with wood since the age of 16 yr. Tumor types were limited to glandular (secreting) carcinoma (16/17) and reticulosarcoma (1/17). There were no instances of cancer of the maxillary sinus alone, and the ethmoid sinus appeared to be the original site of cancer in all cases. Among the 36 other pts. presenting with ethmoid or ethmoid + maxillary tumors, tumor types included spinocellular carcinoma (16/36; 7/16 male), glandular (secreting) carcinoma (12/36; 10/12 male), lymphosarcoma (3/36; all male), basocellular carcinoma (2/36; all male), and 1 case (each) of papillary carcinoma, cylindroma, and malignant plasmacytoma (all male).

70-369 ACUTE ERYTHROLEUKEMIA INDUCED BY BENZENE. (Fr.) Bryon, P.-A., P. Coeur, R. Girard, O. Gentilhomme and L. Revol.
J. Med. Lyon 50(1164):757-759, 1969.

A 55-yr.-old man had been using a solvent containing 33% benzene, 67% toluene, daily for 20 yr. in dissolving rubber at a temperature of approximately 100° C. He presented with a history of progressive asthenia during the past 5 mo., dyspnea on effort for 2 mo., and a temperature of 38.5° C for a week. Examination, including bone marrow biopsy, confirmed that the pt. was suffering from severe anemia, acute, malignant erythroblastosis, and medullary insufficiency, accompanied by the proliferation of

myeloblasts in both the circulating blood and the marrow. The pt. was resistant to treatment with 6-mercaptopurine and methylprednisolone hemisuccinate, and died 4 mo. after the initial diagnosis.

70-370 A PROLIFERATIVE MYELOSIS WITH RAPID EVOLUTION. POSSIBLE ETIOLOGIC ROLE OF CHLORINE DERIVATIVES OF BENZENE. (Fr.) Tolot, F., B. Soubrier, J.-R. Bresson and P. Martin.
J. Med. Lyon 50(1164):761-768, 1969.

A 40-yr.-old dye worker had a history of 22 yr. of mixing and dissolving powdered dyestuffs at 100° C and then carrying them into a small, unventilated room where he added the mixtures to fabrics which were being treated with several compounds, one of which had orthodichlorobenzene as a solvent. He presented with severe anemia, purpura of the lower extremities, and several weeks' history of progressive asthenia and dyspnea on effort. Examination, including bone marrow biopsy, confirmed that he was suffering from acute erythroblastosis in the presence of global medullary insufficiency and a myelo-proliferative syndrome characterized by the presence of immature myelocytes in the peripheral circulation, extensive myelofibrosis, and incipient megakaryocytic aplasia. Methemoglobinemia was 8%, with paraminophenol demonstrable in the urine, appearing to confirm a complex, chronic intoxication of occupational origin, involving coloring or other compounds containing aromatic amines and possibly also involving the solvent, orthodichlorobenzene, although neither benzene nor toluene were demonstrable in the blood and trichloroacetic acid was not demonstrable in the urine. The pt. was resistant to androgens and corticosteroids and died 4 mo. after seeking medical assistance.

70-371 SERIOUS BLOOD DISORDERS AND EXPOSURE TO CHLORINE DERIVATIVES OF BENZENE. (A REPORT OF 7 CASES). (Fr.) Girard, R., F. Tolot, P. Martin and J. Bourret.
J. Med. Lyon 50(1164):771-773, 1969.

Eight illustrative case histories are cited. A 70-yr.-old woman developed severe anemia and medullary aplasia, traced to her employment as a cottage worker, gluing hats together with a compound containing 70% monochlorobenzene. A 53-yr.-old shoe manufacturer developed chronic lymphatic leukemia with peripheral and abdominal lymphadenopathies and hepatosplenomegaly after 16 yr. of using glue containing methylethylketone, cyclohexane, and 2% orthodichlorobenzene. A 68-yr.-old woman developed severe aplastic anemia, medullary aplasia, and leuko- and thrombocytopenia, traced to soaking her husband's work clothes in trichlorobenzene before washing them. A 15-yr.-old schoolgirl developed fatal, acute myeloblastic leukemia with a unilateral retroclavicular lymphadenopathy and peripheral

leukoblastosis, traced to constantly "spotting" her clothes, without removing them, with a product containing 37% orthodichlorobenzene. A 40-yr.-old workman developed chronic lymphatic leukemia with peripheral lymphadenopathies after 10 yr. of cleaning electrical contacts with a solvent containing 80% ortho-, 2% meta-, and 15% paradichlorobenzene. A 55-yr.-old woman developed acute myeloblastic leukemia after an unspecified period of using the same solvent to "spot" her own, her husband's, and her children's clothing. A 40-yr.-old man developed an acute myeloproliferative syndrome, traced to his frequent occupational use of orthodichlorobenzene. A 40-yr.-old man developed anemia suddenly after 3 yr. employment filling drums with mono-, ortho- and trichlorobenzene manually, injecting steam in cold weather to keep the compounds from crystallizing. Prior to entering this employment, he had been exposed to DDT for 30 years.

70-372 THE FREQUENCY OF UNRECOGNIZED EXPOSURE TO BENZENE IN PATIENTS WITH SERIOUS HEMATOLOGIC DISORDERS. (REPORT OF AN INQUIRY MADE OF 200 HOSPITALIZED PATIENTS.). (Fr.) Revol, L. and R. Girard. *J. Med. Lyon* 50(1164): 91-797, 1969.

During a 14-mo. period, all pts. admitted to a Lyon hospital with certain, specified hematologic disorders (see below) were questioned concerning possible history of exposure to benzene or toluene. In all, 17/200 answers were positive, with 14/17 verified objectively by chemical analysis of products or manufacturers' statements of content. Occupational exposures accounted for 14/17, with 6/17 involving the use of paints and varnishes, 4/17 the removal of grease spots from clothing, 3/17 gluing shoes, 2/17 gluing food and 2/17 cleaning mechanical apparatus. Unconfirmed and probable cases were tabulated by disorder, as follows (numbers in parentheses show the total number of cases hospitalized during the study period): acute leukemia (70) = 1 and 1, resp.; chronic lymphatic leukemia (32) = 1 and 1, resp.; chronic myeloid leukemia (30) = 1 and 0, resp.; medullary aplasia (17) = 3 and 0, resp.; mono- or bicytopenia (27) = 1 and 0, resp.; myeloid splenomegaly (7) = 1 and 0, resp.; reticulo- or lymphosarcoma (17) = 0 and 1, resp. In 8 additional cases of leukemia (7/8, acute; 1/8, chronic myeloid), the pts. had painted their buildings several mo. before the first symptoms appeared, but samples of the varnishes, paints, and thinners used could not be obtained and manufacturers' statements of content could not be ascertained. Among 8 pts. in whom it was determined, WBC alkaline phosphatase activity was low in 2 with acute leukemia and 1 (each) with myeloid splenomegaly and chronic myeloid lymphatic leukemia. It was normal in 2 pts. with acute leukemia and increased in 1 pt. with reticulosarcoma.

70-373 CYTOLOGY AND ENZYME HISTOCHEMISTRY OF SQUAMOUS CARCINOMA OF THE HAMSTER CHEEK POUCH AND HUMAN ORAL MUCOSA. (E.) Oka, R. (Osaka U. Dent. Sch., Japan). *Gann* 60(6): 631-648, 1969.

Exfoliated cells and sections from hamster cheek pouch mucosa were studied during various stages of 7,12-dimethylbenzanthracene carcinogenesis. Specimens of normal human oral mucosa (from 25 subjects) and squamous cell carcinomas of the oral cavity (28 pts.) were also examined. No marked variations from normal to malignant tissues, with respect to the enzyme staining reactions, were seen in the histological sections. Enzyme reactions were less intense in the exfoliated cells than in the histological sections. Exfoliated tumor cells tended to show a negative alkaline phosphatase reaction, a weak nonspecific esterase reaction, and intense reactions for lactate, malate and glucose-6-phosphate dehydrogenases. This combination of reactions was of diagnostic value for carcinoma, as was the percentage distribution of exfoliated cells showing weak non-specific esterase and intense lactate and malate dehydrogenase activities. Acid phosphatase and succinate dehydrogenase activities were of less diagnostic value.

70-374 CYTOGENETIC ANALYSIS OF CELL POPULATIONS IN RAT LEUKEMIA INDUCED BY PULSE DOSES OF 7,12-DIMETHYLBENZ[a]ANTHRACENE. (E.) Kurita, Y. (Aichi Cancer Ctr. Res. Inst., Nagoya, Japan), T. Sugiyama and Y. Nishizuka. *Gann* 60(5):529-535, 1969.

Frequencies of karyotypically distinct cell populations were studied in 93 primary leukemias (selected at random) induced in Long-Evans rats by pulse doses of 7,12-dimethylbenzanthracene. These leukemias showed a wide variety of chromosomal abnormalities. Cells with a normal diploid karyotype were seen in 91/93 leukemias (97.9%), but most leukemias showed 1 or more karyotypically distinct cell populations, indicating multiple clonal origin of the leukemic cells. Examination of stemline cells in each leukemia showed trisomy of the largest telocentric chromosome (C-1) in 32/103 stemlines (31.1%) and the normal karyotype in 48/103 stemlines (46.6%) examined. The cells with C-1 trisomy were in various stages of maturation toward erythroblasts, whereas the cells of normal karyotype constituted several types of leukemia. It is suggested that the chromosomes of the leukemic cells of normal karyotype may show quantitative and qualitative changes in the DNA component of the genomes, which would result in an abnormal phenotypic expression.

70-375 PREVENTION BY SPIRONOLACTONE OF 7,12-DIMETHYLBENZ[a]ANTHRACENE-INDUCED

ADRENAL NECROSIS. (E.) Kovacs, K. (U. Montreal Inst. Exp. Med. Surg., Canada) and A. Somogyi. Proc. Soc. Exp. Biol. Med. 131(4):1350-1352, 1969.

In female Sprague-Dawley rats admin. 1 dose of 7,12-dimethylbenzanthracene (DMBA; 40 mg p.o.), treatment with spironolactone (S; 10 mg twice daily x 6 days, beginning 2 days before DMBA admin.) completely inhibited the development of adrenal necrosis. By 4 days after DMBA admin., 25/30 DMBA-treated rats and 0/30 rats admin. DMBA + S had developed adrenal necrosis. Admin. of S also inhibited the development of adrenal necrosis in rats admin. the same dose of DMBA i.v., which excluded the possibility of a local chemical interaction between DMBA and S in the g.i. tract.

70-376 MAMMARY CANCER INDUCTION BY 7, 12-DIMETHYLBENZ[a]ANTHRACENE: RELATION TO AGE. (E.) Dao, T. L. (Roswell Park Mem. Inst., Buffalo, N. Y.). Science 165(3895):810-811, 1969.

Mammary glands from inbred female Wistar-Furth rats, admin. 7,12-dimethylbenzanthracene (DMBA; 3 mg/100 g x 1 i.v.) at age 56 or 120 days, were transplanted 30 min.-20 days later into 56- or 120-day-old recipients. In recipients of either age, tumor development in grafts from the younger donors was much better than in the grafts from the older donors, suggesting that the most important factor in DMBA carcinogenesis in rat mammary grafts is the age of the graft, not the age of the recipient. Similar results were seen when the recipients received DMBA 2 wk. after implantation of mammary grafts from untreated donors. The age-related susceptibility to DMBA could not be explained by the presence of marked morphological differences in the mammary glands. No significant morphological differences were seen between the mammary glands of 56- and 120-day-old rats, except for a more extensive lobulo-alveolar proliferation in most of the younger animals.

70-377 DEPRESSIVE EFFECT OF BONE MARROW ON THE YIELD OF 7,12-DIMETHYLBENZ[a]ANTHRACENE-INDUCED THYMIC LYMPHOMAS. (E.) Ball, J. K. (U. Western Ontario, London, Canada). J. Nat. Cancer Inst. 44(2):439-445, 1970.

In CFW/D mice inj. neonatally with 7,12-dimethylbenzanthracene (DMBA; 30 µg s.c.), admin. of $1-6 \times 10^7$ normal bone marrow cells (BMC) from syngeneic mice reduced the lymphoma frequency by 30-50%, if the BMC were admin. 7-10 days after DMBA. Admin. of BMC 3-5 days or 21 days after DMBA did not affect the lymphoma yield. BMC admin. was effective by both the i.v. and i.p. routes. After i.v. inj. of BMC, the mice showed a marked increase in the cellularity of both the bone marrow and the thymus; after i.p. inj. of

BMC, only the thymus showed an increase in cellularity.

70-378 POLYINOSINIC-POLYCYTIDYLIC ACID INHIBITS CHEMICALLY INDUCED TUMOR-IGENESIS IN MOUSE SKIN. (E.) Gelboin, H. V. (NCI, Bethesda, Md.) and H. B. Levy. Science 167(3915):205-207, 1970.

Skin tumors were induced in NIH Swiss mice with topically applied 7,12-dimethylbenzanthracene (DMBA) and promoted to the visible stage by weekly applications of croton oil. Polyinosinic: polycytidylic acid (poly I:C), given i.p. before and after the DMBA had little or no inhibitory effect; when given during treatment with croton oil, tumor formation was suppressed, but resumed upon its withdrawal; when given after a single large dose of DMBA, tumor development was suppressed up to 18 weeks.

70-379 THE CONVERSION OF PHENANTHRENE 9,10-OXIDE AND DIBENZ[a,h]ANTHRACENE 5,6-OXIDE INTO DIHYDRODIOLS BY A RAT-LIVER ENZYME. (E.) Pandov, H. (Oncol. Res. Inst., Sofia, Bulgaria) and P. Sims. Biochem. Pharmacol. 19(1):299-303, 1970.

In rat liver homogenates, the enzyme catalyzing ³H-labeled phenanthrene-9,10-oxide (PO) to its dihydrodiol (9,10-dihydro-9,10-dihydroxyphenanthrene) was localized predominantly in the microsomal fraction. PO was a much better substrate for this enzyme than dibenz(a,h)anthracene-5,6-oxide (DBAO; converted to 5,6-dihydro-5,6-dihydroxybenz(a,h)anthracene). This difference in dihydrodiol formation could not be explained by the lesser solubility of DBAO in aqueous media. No more than 75% of the added PO was converted into the dihydrodiol by rat liver microsomes; the remainder was probably converted into 9-phenanthrol by a non-enzymatic rearrangement. Liver homogenates yielded less dihydrodiol from PO than an equivalent wt. of microsomes; it is suggested that some of the PO may be metabolized by an alternative pathway involving conjugation with glutathione.

70-380 RATE OF RIBONUCLEIC ACID SYNTHESIS IN MOUSE SKIN, FOLLOWING TOPICAL APPLICATION OF 3,4-BENZOPYRENE. (Fr.) Alexandrov, K. (Cancer Res. Inst., Villejuif, France), R. Vendrely and C. Vendrely. C. R. Soc. Biol. (Paris) 163(1):29-33, 1969.

Three days after shaving, 6-10-week-old, male IC mice were treated by topical application to the back with 3,4-benzopyrene (BP) in acetone, 1/2, 1, 2, 3, 4 and 24 hours prior to sacrifice. Tritiated cytidine (10 µC/g) was inj. 30 min. prior to sacrifice. Autoradiography confirmed that during the first 2 hours after applying BP, the incorporation of cytidine into the skin

decreased rapidly to 75% normal levels; returned to normal by the third hour; then increased rapidly and progressively, to exceed 150% normal levels by the twenty-fourth hour. The effect was somewhat more marked in the cells of the sebaceous glands than in the epidermal cells. Electrophoretic studies at 2, 26 and 40 hours after BP application showed that the relative distribution of the 3 RNA fractions was not affected significantly, as compared to untreated controls.

0-381 ENZYMATIC HYDROXYLATION OF BENZOPYRENE AND ITS RELATIONSHIP TO CYTOTOXICITY. (E.) Gelboin, H. V. (Weizmann Inst. Sci., Rehovoth, Israel), E. Huberman and L. Sachs. Proc. Nat. Acad. Sci. USA 64(4):1188-1194, 1969.

Various normal and transformed hamster, mouse and human cell cultures were pretreated with benzo(a)anthracene (10 µg/ml, to induce maximal enzyme) and assayed for aryl hydrocarbon hydroxylase. Cell susceptibility to the cytotoxic effect of benzo(a)pyrene (BP; 10 µg/ml) correlated with enzyme levels, indicating that cytotoxicity is due to enzymatic conversion of benzo(a)pyrene to cytotoxic products. While BP was toxic mainly to normal cells, 3-hydroxybenzo(a)pyrene, a product of enzymatic hydroxylation of BP, was toxic to normal and to a greater extent, transformed cells. Susceptible transformed cells may occasionally give rise to variant resistant transformed cells lacking the microsomal enzyme.

0-382 SPECIFIC GENETIC DELETIONS BY A CARCINOGENIC HYDROCARBON IN Drosophila. (E.) Fahmy, O. G. (Chester Beatty Res. Inst., London) and M. J. Fahmy. Nature (London) 224(5226):1328-1329, 1969.

Specific mutability tests with various carcinogens are performed on X chromosome loci in male Drosophila, including the white, forked, maroon-eye, and bobbed loci. Inj. of 7,12-dimethylbenzo(a)anthracene into the hemocoel of adult flies induced a significantly elevated incidence of mutation at the bobbed locus.

0-383 THE METABOLISM OF SOME AROMATIC HYDROCARBONS BY MOUSE EMBRYO CELL CULTURES.

(E.) Sims, P. (Chester Beatty Res. Inst., London). Biochem. Pharmacol. 19(1):285-297, 1970.

Primary mouse embryo cell cultures exposed to labeled aromatic hydrocarbons, no "K-region" hydrodiols were formed from 7,12-dimethylbenzo(a)anthracene (DMBA), 7-methylbenzo(a)anthracene (MeBA), 7-bromomethylbenzo(a)anthracene (7-BrMeBA) benzo(a)pyrene (B(a)P). DMBA was converted to its 8,9-dihydrodiol and into the 8,9-dihydrodiols of the corresponding hydroxymethyl derivatives. The methyl groups were also

oxidized into carboxylic acids. The metabolic conversion of 7-MeBA resembled that of DMBA, while 7-BrMeBA yielded mostly 7-hydroxymethylbenzo(a)anthracene (probably by a non-enzymatic reaction). B(a)P was converted into 3-hydroxy-, 1,2-dihydro-, 1,2-dihydroxy- and 9,10-dihydro-9,10-dihydroxy-B(a)P. In mouse embryo cells and rat liver homogenates, benzo(e)pyrene was converted to a phenol and to a "K-region" dihydrodiol. The mouse embryo cells also converted all of these hydrocarbons into unidentified water-soluble metabolites.

70-384 TRANSPLANTATION TECHNIQUE FOR ACCELERATION OF CARCINOGENESIS BY BENZ[a]-ANTHRACENE OR 3,4,9,10-DIBENZOPYRENE[BENZO(rst)PENTAPHENE]. (E.) Homburger, F. (Bio-Res. Inst., Cambridge, Mass.) and A. Treger. J. Nat. Cancer Inst. 44(2):357-360, 1970.

When multiple injection sites of 3,4,9,10-dibenzopyrene (DBP; 25 µg) or benzo(a)anthracene (BA; 500 µg), pooled from 4 male C57BL/6J mice, were transplanted into 1 mouse each of the same sex and strain, the secondary hosts developed palpable tumors in about half the time required for the development of tumors induced by s.c. inj. of DBP or BA. When site transfers were made 8-24 wk. after BA admin., the tumor yield was significant within 24 wk. after the original inj., whereas tumors developed in only 2/48 mice treated with BP and observed for 52 wk. after the original inj. When site transfers from BA-treated mice were made 8 or 12 wk. after the first inj., 67% and 80% of the transplants, resp., yielded tumors by 24 wk. after the first inj. Tumor yields were lower when site transfer was delayed for 16 or 24 wk. In mice transplanted with sites inj. with DBP 6 wk. previously, the first tumor appeared 9 wk. after the original inj., whereas the first tumor in mice treated with DBP developed 12 wk. after a single inj. of the carcinogen.

70-385 SARCOMA-PRODUCING CELL LINES DERIVED FROM CLONES TRANSFORMED IN VITRO BY BENZO[a]PYRENE. (E.) DiPaolo, J. A. (NCI, Bethesda, Md.), R. L. Nelson and P. J. Donovan. Science 165(3896):917-918, 1969.

Primary or secondary cultures of Syrian hamster embryonic cells, exposed for 10 days to 3,4-benzopyrene (0.1-10 µg/ml), yielded transformed clones, 8 of which were used to establish permanent cell lines. Transplantable fibrosarcomas developed in hamsters inj. (s.c. or intradermally) with cells from 7/8 of these cell lines. The 10 control cell lines, derived from hamster embryonic cells exposed to pyrene, did not produce tumors in hamsters. The transformed cells were negative in complement-fixation tests for antigens of oncogenic viruses known to transform hamster cells in vitro or in vivo.

70-386 THE SARCOMA-INDUCING EFFECTS OF TWO NITROGEN DERIVATIVES OF 3,4,9,10-DIBENZPYRENE. (Fr.) Giau, N.-B. (Inst. Radium, Paris) and N. P. Buu-Hoi. Bull. Cancer (Paris) 55(4):531-534, 1968.

In 5-6-mo.-old XVII line (Radium Inst.) mice receiving 5-amino-3,4,9,10-dibenzpyrene (1 mg/dose x 3, s.c. in neutralized olive oil at 30-day intervals), 1/6 males and 4/6 females developed fibrosarcomas with latency periods of 218 days and 184-358 days, resp. The remaining animals died spontaneously, without cancer, after 142-308 days. In animals receiving identical treatment with 5-nitro-3,4,9,10-dibenzpyrene, 2/6 males and 0/6 females developed sarcomas, with latency periods of 355-474 days for the 2 males. The remaining animals died spontaneously, without cancer, after 143-416 days. It was concluded that the amino compound was the more active, but that both were considerably less active than the parent compound, as was true of previously reported attempts to introduce a substitute into the hydrocarbon molecule.

70-387 THE REACTION OF IMIDAZOLE COMPOUNDS WITH 3,4-BENZPYRENE, AND ITS EFFECTS ON THE FORMATION AND FUNCTIONING OF NUCLEIC ACIDS. (Fr.) Champy-Hatem, S. Bull. Acad. Nat. Med. (Paris) 153(9-10):140-145, 1969.

In UV spectroscopic studies, a reaction between 3,4-benzpyrene (BP) and the imidazole molecule could not be achieved in an acid medium. Imidazole did react with BP in an alkaline medium, and the reaction was particularly strong at the pH of normal human tissue, disappearing again at pH 3. When the BP-imidazole reaction was slowly reduced to zero by altering the pH of the medium, a weak but demonstrable BP-2-methylimidazole reaction could still be demonstrated, due to sensitization of the alkaline nitrogen function of imidazole by the placement of the methyl group. The reaction BP-N-methylimidazole under the same conditions of pH was intense, due to blocking of the hydrogen on the nitrogen of imidazole, although N-methylimidazole failed to react to any appreciable extent with the carcinogenically-inactive structural analogs of BP. It was concluded that it is the alkaline nitrogen function of imidazole which attaches itself to the carcinogen, a reaction which is intensified when the hydrogen on the nitrogen is blocked, as it is in the course of nucleic acid synthesis, when the purine base is attached to the carbohydrate.

70-388 IN VITRO MALIGNANT TRANSFORMATION BY METHYLCHOLANTHRENE OF THE PROGENY OF SINGLE CELLS DERIVED FROM C3H MOUSE PROSTATE. (E.) Mondal, S. (U. Wisconsin McArdle Lab. Cancer Res., Madison) and C. Heidelberger. Proc. Nat. Acad. Sci. USA 65(1):219-225, 1970.

Methylcholanthrene (MCA) and dimethyl sulfoxide (DMSO) were added to single cells of a cell line

derived from C3H mouse ventral prostate, and the cells were observed for transformation. Clones derived from cells treated with DMSO (0.5%) showed 6% transformation; optimal concentrations of MCA (1.0 - 2.5 µg/ml for 6 days) yielded 100% transformation in 81 days. Cells cloned before treatment (1 µg/ml MCA for 24 hr.), and recloned 8 days after treatment all demonstrated transformation by the 77th day (35/35), while there was no incidence (0/34) of transformation among those treated with DMSO. These results indicate that the carcinogen does not select for pre-existing malignant cells. Individual cells were also cloned after treatment with 1 µg/ml MCA, but before showing transformation; of these, 100% had piled up colonies by the 44th day. Thus all progeny contained the potential for transformation.

70-389 IMMUNOLOGIC SURVEILLANCE AT THE MACROSCOPIC LEVEL: NONSELECTIVE ELIMINATION OF PREMALIGNANT SKIN PAPILLOMAS. (E.) Lappé, M. A. (U. California, Berkeley) and R. T. Prehn. Cancer Res. 29(12):2374-2378, 1969.

In BALB/cAn mice bearing syngeneic grafts of 3-methylcholanthrene-initiated skin, significantly more carcinomas developed from papillomas on grafts carried by immunologically incompetent hosts (treated by thymectomy or sham-thymectomy + total-body irradiation) than from papillomas on grafts in immunologically competent or BCG-stimulated hosts. The number of carcinomas in each treatment group was inversely proportional to the host animals' ability to cause regression of the papillomas. Carcinomas appeared earlier and in larger numbers when papilloma regression was delayed by long-term immunological impairment, than in immunologically competent animals showing more rapid rates of papilloma regression. The rate of malignant progression was constant, independent of papilloma regression. It is suggested that immunological surveillance can act at the macroscopic level to reduce the risk of malignancy, only to the extent that such surveillance reduces the total number of days when papillomas are present.

70-390 CARCINOGENESIS OF THE PROSTATE IN ALBINO RATS, INDUCED BY 3-METHYLCHOLANTHRENE. (It.) Ronzoni, G. (Catholic U. Sacred Heart Inst. Clin. Surg., Rome), P. Alquati, P. Pola and E. Alcini. Chir. Pat. Sper. 16(5):435-444, 1968.

When crystals of 3-methylcholanthrene (10 mg, single dose) were injected into the prostate glands of adult Wistar rats, 89/182 animals surviving surgery developed prostatic cancers, consisting of adenocarcinomas (24/89), sarcomas (16/89) and squamous cell carcinomas (49/89). The latency periods were 4-5 mo., 7-8 mo. and 5-6 mo., resp. Among animals serving as controls, the frequency of cancerization was 55%. Among animals treated intercurrently with

estradiol benzoate or cortisone, it was 80% and 70%, resp. Among those treated with ACTH or triiodothyronine, it was 30%. Among those treated with 19-nortestosterone phenylpropionate or progesterone, it was 40%. Intercurrent treatment with testosterone propionate, methylthiouracil or bilateral orchiectomy failed to influence cancerization significantly (= 53.3%, 50% and 50%, resp.). All intercurrent medications were admin. i.m. Dosage was 10 mg/2 weeks, except for testosterone propionate (25 mg/2 weeks) and progesterone (5 mg/2 weeks).

70-391 INCREASED ONCOGENIC EFFECT OF METHYLCHOLANTHRENE AFTER TREATMENT WITH ANTI-LYMPHOCYTE SERUM. (E.) Balner, H. (Radiobiol. Inst. TNO, Rijswijk, Netherlands) and H. Dersjant. *Nature (London)* 224(5217):376-378, 1969.

Female (CBA x C57Bl)F₁ mice were treated i.p. with antilymphocyte serum (ALS) of horse or rabbit origin for 5 or 9 wk., resp., beginning at 12 wk. of age. One intracutaneous inj. of 3-methylcholanthrene (MC; 0.05 mg) was admin. 1 wk. after the start of ALS admin. Controls were treated with MC alone or with normal horse or rabbit serum (1 group received an ineffective horse ALS). The effects of the horse and rabbit immune sera were about the same. In the 2 groups combined, the tumor incidence in the 4-mo. survivors was 80% with MC + ALS, 40% with MC alone and 20% with MC + normal serum. The normal serum apparently delayed the appearance of tumors slightly. This difference between ALS-treated mice and controls was also evident at 6 mo., but no significant difference was seen thereafter. No tumors developed at any time in mice treated with ALS only. Since early chemically-induced tumors show particularly high levels of antigenicity, it is suggested that the growth potential of these tumors can override the weakened host defenses of the ALS-treated mice, whereas control mice can reject such highly antigenic tumors.

70-392 TUMOUR SPECIFIC TRANSPLANTATION ANTIGENS: POSSIBLE ORIGIN IN PRE-MALIGNANT LESIONS. (E.) Lappé, M. A. (U. California, Berkeley). *Nature (London)* 223(5201):32-84, 1969.

A papilloma induced in an adult female BALB/cAnNcr mouse by implantation of a 3-methylcholanthrene (10% in paraffin)-impregnated Millipore filter disk (for 30 days), was serially transplanted into sublethally irradiated and non-irradiated adult female BALB/c mice. The referential growth of the papilloma in the irradiated mice, and its ability to stimulate specific radiation-resistant immunity in these hosts, were used as criteria for the immunogenicity of the tumor. A carcinoma derived from this papilloma shared a common antigenicity with the papilloma. The poorer sensitization conferred by the papilloma (compared to the carcinoma)

was attributed to the poorer growth rate of sensitizing implants of the papilloma, rather than to a qualitative difference in antigenicity.

70-393 CARCINOGEN-INDUCED IMMUNE DEPRESSION: ABSENCE IN MICE RESISTANT TO CHEMICAL ONCOGENESIS. (E.) Stutman, O. (U. Minnesota Coll. Med., Minneapolis). *Science* 166(3905):620-621, 1969.

A single dose of 3-methylcholanthrene (MC; 0.1 mg), admin. s.c. to 35-day-old male C3Hf/Bi or I mice, induced local tumors in 50/50 (100%) and 10/87 (11%), resp., by 240 days later. The immunological response to sheep RBC was markedly inhibited by pretreatment with MC in the sensitive C3Hf/Bi mice, but MC had no immunosuppressive effect in the I mice, even in newborn animals. The data were consistent with the possibility of host immune mechanisms as regulators of malignant development. However, since the I mice were not absolutely resistant to MC tumor induction, and since MC was not immunosuppressive even in tumor-bearing I mice, it is also suggested that paraimmunological and non-immunological mechanisms may also be involved.

70-394 METASTASIZING MAMMARY CARCINOMAS IN RATS: INDUCTION AND STUDY OF THEIR IMMUNOGENICITY. (E.) Kim, U. (Roswell Park Mem. Inst., Buffalo, N. Y.). *Science* 167(3914):72-74, 1970.

Mammary tumors induced by 3-methylcholanthrene fed (200 mg over a 5-week period) to splenectomized and/or thymectomized W/Fu rats (50-day-old, female) were excised and transplanted in 3-6 young adult female syngeneic rats. The thymectomy-derived mammary carcinoma showed preferential pulmonary metastases, and all were well-differentiated adenocarcinomas, with those from splenectomized and the splenectomized-thymectomized rats tending to become undifferentiated with increasing transplantation generations. Immunization (intradermal) of young adult rats with X-irradiated cells of metastatic tumors failed to protect against injection with corresponding tumor cells, whereas nonmetastasizing tumors were completely suppressed, suggesting that the metastasizing tumors are less immunogenic.

70-395 ANTIGENIC STRUCTURE OF AZO-INDUCED HEPATOMAS IN THE WISTAR RAT. I. DEMONSTRATION OF SEVERAL TUMOR-SPECIFIC ANTIGENS. (Fr.) Capron, A. (Inst. Cancer Res., Lille, France), A. Vernes, A. Demaille, L. Adenis and J. Driessens. *C. R. Soc. Biol. (Paris)* 163(7):1551-1553, 1969.

In tumor tissue from the livers of adult Wistar rats of both sexes in which hepatomas were induced by prolonged p.o. admin. of 4-dimethylamino-3'-methylazobenzene, repeated immuno-electrophoretic studies confirmed the presence

of 18 antigen fractions, in contrast to the 24 fractions which were demonstrable in normal rat liver tissue. Three of these were characterized by the formation of corresponding precipitins in hyperimmunized rabbits, and appeared to be specific for hepatoma tissue.

70-396 ON RELATIONSHIPS BETWEEN INDUCTION OF LIVER CANCER WITH AZO DYES AND CHANGES IN NUCLEAR RNA METABOLISM DURING CARCINOGENESIS. (E.) Kizer, D. E. (Samuel Roberts Noble Found., Ardmore, Okla.) and J. A. Clouse. Proc. Soc. Exp. Biol. Med. 132(3):1174-1177, 1969.

Patterns of incorporation of ^{14}C -labeled orotic acid and adenine into nucleolar and non-nucleolar nuclear RNA of the liver were studied in female Holtzman rats, fed diets containing 0.06% 3'-methyl-4-dimethylaminoazobenzene (MeDAB) or 4'-fluoro-4-dimethylaminoazobenzene (F-DAB) for 12 wk. No liver tumors were seen in 24 rats fed F-DAB in Farber's diet (low-riboflavin), but 10/11 developed tumors after admin. of F-DAB in Medes' diet (high-riboflavin). MeDAB induced liver tumors in essentially all animals, irrespective of the diet. No appreciable changes were seen in the RNA contents of either nucleolar or non-nucleolar nuclear RNA in the livers of carcinogen-treated rats. No consistent relationship was seen between liver tumor induction and changes in the patterns of precursor incorporation into either RNA fraction.

70-397 CARCINOGEN IN A TRANSKEIAN BANTU FOOD ADDITIVE. (E.) DuPlessis, L. S. (Rhodes U., Grahamstown, South Africa), J. R. Nunn and W. A. Roach. Nature (London) 222(5199): 1198-1199, 1969.

Dimethylnitrosamine was isolated from the fruit of the solanaceous bush (*Solanum incanum*) in the Transkei, South Africa and identified by chromatography and nuclear magnetic resonance. The high incidence of esophageal cancer among Transkeian Bantu may be attributable to this agent. The Bantu use the juice to curdle milk which is the chief food for the first twenty years of life.

70-398 CARCINOGENIC RESPONSE OF THE HAMSTER RESPIRATORY TRACT TO SINGLE SUBCUTANEOUS ADMINISTRATIONS OF DIETHYLNITROSAMINE AT BIRTH. (E.) Montesano, R. and U. Saffiotti (NCI, Bethesda, Md.). J. Nat. Cancer Inst. 44(2):413-417, 1970.

A single s.c. inj. of diethylnitrosamine (DENA) was admin. to 4 groups of random-bred newborn Syrian golden hamsters; 144/204 survived 5 weeks or more (max. about 109 weeks). The overall tumor incidence was about the same in males and in females. Among the 5-week survivors admin. DENA doses of 15, 30, 90 and 150 μg (corresponding to 5.5, 11, 33 and 55 mg/kg,

resp.), tumors developed in 22/37, 23/48, 22/33 and 19/26, resp. Respiratory tumors developed in 19/22, 23/23, 21/22 and 18/19 of the tumor-bearing animals, resp. (30-65% of each dosage group). Polyps and/or papillomas of the trachea and larynx (69/81 and 27/81 respiratory tumors, resp.), without invasiveness or metastases, developed after av. latent periods of 70-80 weeks in all dosage groups. Nasal cavity tumors developed in 10 animals (4 neuroepithelial tumors, 1 squamous cell papilloma, 2 adenocarcinomas, 3 anaplastic carcinomas), bronchial polyps in 5, and lung tumors in 4 (2 benign adenomas, 2 small cell anaplastic carcinomas). A total of 17-nonrespiratory tumors (6 forestomach papillomas, 4 lymphomas, 3 adrenocortical adenomas, 2 liver tumors, 1 melanoma, 1 cheek pouch papilloma) developed in 15/144 of the 5-week survivors. Many treated animals developed biliary cysts and proliferative changes of the liver. Untreated animals from the authors' colony showed no spontaneous respiratory tumors.

70-399 IMMUNOLOGICAL DEFENCE AGAINST PRE-NEOPLASTIC STAGES OF DIETHYLNITROSAMINE INDUCED CARCINOMAS IN RAT LIVER. (E.) Friedrich-Frekxa, H. (Max Planck Inst. Virus Res., Tubingen, Germany) and M. Hoffmann. Nature (London) 223(5211):1162-1163, 1969.

In rats treated with diethylnitrosamine (DENA) in a dose which induces liver carcinomas at least 6 mo. after the beginning of treatment (8 mg/kg/day x 6 weeks), the development of pre-neoplastic liver islets after DENA admin. was initially enhanced by admin. of a 6-week course of rabbit anti-rat lymphocyte serum (ALS; 1.0 ml x 1, then 0.5 ml/day). The effect of ALS was no longer evident by 5 weeks after the end of ALS admin. Normal rabbit serum had no effect. It is concluded that the latent stage of liver carcinoma development represents an immunological defense mechanism against the premalignant lesions.

70-400 HISTOCHEMICAL INVESTIGATIONS OF CARCINOGENESIS IN RAT LIVER AFTER TIME-LIMITED APPLICATION OF DIETHYLNITROSAMINE. (Ger.) Friedrich-Frekxa, H. (Max Planck Inst. Virus Res., Tubingen, Germany), G. Papadopolu and W. Gössner. Z. Krebsforsch. 72(3):240-253, 1969.

Forced feeding of thioacetamide (TAA) or diethylnitrosamine (DENA) to female Sprague-Dawley rats (150-250 g) in 8 mg/kg/day dose for 2-10 weeks resulted in the appearance of clear areas around the central vein in both groups. This effect was reversible and disappeared a few weeks after discontinuation of feeding. In contrast to this, DENA also induced after 4 wk admin. (total 224 mg) irreversible islands of cells lacking glucose-6-phosphatase activity while TAA did not (even after 10 weeks of feeding).

The persistence of these islands was shown by admin. of DENA in 8 mg/kg/d for 1 week (total 56 mg/kg) and examination of livers 8-210 days later. A micro-carcinoma was found after 168 days and several islands were still present after 210 days. The growth and transformation of islands was followed by feeding DENA for 8 weeks (total 448 mg/kg) and calculating the island/total liver tissue ratio 3-12 weeks later or histochemical examination 6 mo. later. The islands did not grow for 5 weeks but then suddenly increased in size and some transformed into carcinomas. Examination (6 mo. after a total dose of 448 mg/kg) of 26 tumors induced in 15/18 rats showed different degrees and combinations of losses of ATPase, glucose-6 phosphatase, acid and alkaline phosphatase, tissue-specific microsomal antigens and glycogen (PAS) in different carcinomas. It is suggested that in order to induce hepatic carcinoma with DENA several somatic mutations are required. Only mutants which increase the rate of cell division of hepatocytes accumulate and this could explain the localization of islands in a sector of the central vein.

70-401 CELL SUSCEPTIBILITY TO THE CYTOTOXIC EFFECT OF THE CARCINOGENS DIMETHYLNITROSAMINE AND N-NITROSOMETHYLUREA. (E.) Huberman, E. (Weizmann Inst. Sci., Rehovoth, Israel), M. Traut and L. Sachs. J. Nat. Cancer Inst. 44(2):395-402, 1970.

Cultures of hamster cells transformed by dimethylnitrosamine (DMNA), benzpyrene (BP) or polyoma virus, showed resistance to the cytotoxic effects of DMNA, whereas normal hamster cells were either susceptible or resistant to DMNA. Some susceptible cells remained in DMNA-exposed cultures, 4 mo. after the DMNA-induced increase in the cellular life span; at later times, resistant cells showing a growth advantage in vitro and in adult hamsters were selected from the population. Unlike DMNA, N-nitrosomethylurea (NMU) was cytotoxic to normal cells and even more cytotoxic to the transformed cells; the different sensitivities of these cells were apparently related to their different growth rates. It is suggested that DMNA is selectively cytotoxic because it must be converted enzymatically to a cytotoxic intermediate, whereas NMU (which seems to be converted non-enzymatically to its cytotoxic intermediate) is not selectively toxic. Unlike BP, DMNA was cytotoxic to normal human cells, but neither agent was cytotoxic to SV40-transformed human cells. This difference suggested that the enzyme involved in the conversion of DMNA to its cytotoxic intermediate is not identical with BP hydroxylase.

70-402 GROSS AND MICROSCOPIC CHANGES IN THE LYMPHORETICULAR SYSTEM DURING GENESIS OF MALIGNANT LYMPHOMA INDUCED BY A SINGLE INJECTION OF METHYLNITROSUREA IN ADULT MICE.

(E.) Joshi, V. V. (U. Western Ontario, London, Canada) and J. V. Frei. J. Nat. Cancer Inst. 44(2):379-394, 1970.

In the thymuses, spleens and lymph nodes of 6-week-old inbred CFW/D mice treated with methyl-nitrosourea (MNU; 75 mg/kg x 1 i.p.), the earliest pathological change noted was cellular depletion, followed by regeneration and then by neoplasia. The earliest neoplastic foci were seen 40 days after MNU admin. The thymus was the site of origin of the lymphomas observed; at least some of these tumors arose by a confluence of 2 or more neoplastic foci. The spleen, lymph nodes and bone marrow were also involved, but this involvement was apparently metastatic. Most of the malignant lymphomas were lymphoblastic, and many showed a "starry-sky" pattern. Lymphoid follicles formed in the thymic medulla during tumor development. The pathological changes observed during tumor development suggested the possibility that a virus might be implicated in the genesis of MNU-induced lymphoma, and that an immunological reaction might be involved in tumor development.

70-403 CYTOGENETIC STUDIES WITH CYCLAMATE AND RELATED COMPOUNDS. (E.) Stoltz, D. R. (Food Drug Directorate Res. Labs., Ottawa, Canada), K. S. Khara, R. Bendall and S. W. Gunner. Science 167(3924):1501-1502, 1970.

Sodium cyclamate, cyclohexylamine sulfate, N-hydroxycyclohexylamine HCl (a metabolite of cyclohexylamine) and dicyclohexylamine sulfate (an occasional contaminant of cyclamate) induced chromosomal damage in cultures of human peripheral WBC. Most chromosomal aberrations were gaps and breaks. Exchange figures and unusual chromosomes of unknown derivation were infrequent, but observed only in treated cultures. The frequencies of chromosomal aberrations were essentially the same after 5 or 25 hours of exposure. These compounds had essentially the same effects on the chromosomes.

70-404 INHIBITION BY 5-FLUOROURACIL OF THE EARLY STAGES OF CHEMICAL CARCINOGENESIS IN MOUSE SKIN. (E.) Olson, P. R. (U. Minnesota Med. Sch., Minneapolis) and L. W. Wattenberg. Proc. Soc. Exp. Biol. Med. 131(4):1135-1137, 1969.

In 2-mo.-old female Ha/ICR mice treated topically with 7,12-dimethylbenzanthracene (DMBA; 200 or 150 µg x 4 over 10 days), followed after 1 or 2 weeks, resp., by topical applications of 5-fluorouracil (FU; 6 days/week x 2 weeks), the latent periods for tumor development were much longer in mice admin. a 1% FU preparation, than in untreated or vehicle (propylene glycol)-treated controls. DMBA carcinogenesis was not inhibited by 0.2% FU or by 1% or 0.2% preparations of cyclophosphamide. In mice with established

skin tumors induced by DMBA (150 μ g \times 4, beginning at age 1 mo.), treatment with 1% FU (12 doses in 2 wk.) caused the regression of 11/13 tumors, whereas an 0.2% FU preparation had no effect.

70-405 INDUCTION OF KIDNEY TUMOURS IN THE RATS BY FEEDING Encephalartos hildebrandtii FOR SHORT PERIODS. (E.) Mugeru, G. M. (Univ. Coll.; Nairobi, Kenya). Brit. J. Cancer 23(4): 755-756, 1969.

Weanling rats were fed basal diets containing a flour prepared from the nuts of Encephalartos hildebrandtii (EH flour; 5%) for 4-28 days and observed for up to 18 mo. No tumors were found in untreated controls or rats admin. EH flour for 4 days. In rats fed EH flour for 7, 14, 21 or 28 days, kidney tumors developed in 12/20, 18/20, 15/20 and 16/20 rats, resp.; 100/107 kidney tumors were classified as adenomas (40), fibrosarcomas (31), nephroblastomas (22) or carcinomas (7). The only kidney tumors which were not also induced by chronic feeding of EH flour were the nephroblastomas. The rats fed EH flour for 21 or 28 days also developed a total of 8 liver tumors (hepatomas, cystadenomas or bile duct adenomas). The large number of kidney tumors and the correspondingly small number of liver tumors seen in this short-term experiment, resembled the results of other experiments using Cycas circinalis meal, cycasin and nitrosamines, and suggested that the carcinogenic factor present in EH flour may be cycasin.

70-406 A TRANSPLANTABLE MYELOMONOCYTIC LEUKEMIA IN BALB/c MICE: CYTOLOGY, KARYOTYPE, AND MURAMIDASE CONTENT. (E.) Warner, N. L. (Hall Inst. Med. Res., Melbourne, Australia), M. A. S. Moore and D. Metcalf. J. Nat. Cancer Inst. 43(4):963-982, 1969.

Treatment with mineral oil (paraffin) and testosterone induced 1 fibrosarcoma, 9 plasma cell tumors and 1 ascites myelomonocytic leukemia (of the chloroma type) in 11/18 BALB/c mice. The myelomonocytic leukemia developed at age 6 mo.; the other tumors developed at age 9-15 mo. The leukemia (designated WEHI-3), when serially transplanted in BALB/c or (BALB/c \times CBA T6T6)F₁ mice, developed into 4 distinct sublines. Two of these sublines retained the original chloroma appearance; 1/2 was diploid and 1/2 was tetraploid. The other 2 sublines were non-chloromatous and 1/2 showed a hypodiploid stemline. The tetraploid subline (WEHI-3D) comprised neoplastic monocytic and granulocytic cells, indicating the existence of a neoplastic stem cell capable of differentiation into both cell series. High levels of muramidase were found in cell suspensions of the solid tumor and in the sera and urine of mice bearing this tumor.

70-407 PRODUCTION OF MOUSE URINARY BLADDER CARCINOMAS BY SODIUM CYCLAMATE. (E.) Bryan, G. T. (U. Wisconsin Med. Sch., Madison) and E. Ertürk. Science 167(3920):996-998, 1970.

Pellets of pure cholesterol or sodium cyclamate suspended in cholesterol were surgically placed in the bladder lumens of duplicate groups of 100 female Swiss mice, 60-90 days old. By 6.6 hr., 99% of the sodium cyclamate eluted from the pellets. The first bladder carcinoma was seen in a cyclamate-fed mouse, 229 days after surgery. The mice exposed to cyclamates had a higher incidence of bladder carcinomas (78 and 61% as opposed to 12 and 13% in the controls); the carcinomas were more often multiple, invasive, and had a high degree of mitotic activity.

70-408 MOUSE LEUKEMIA VIRUS ACTIVATION BY CHEMICAL CARCINOGENS. (E.) Igel, H. J. (Child. Hosp., Akron, Ohio), R. J. Huebner, H. C. Turner, P. Kotin and H. L. Falk. Science 166(3913):1624-1626, 1969.

A rat antiserum against the soluble group-specific antigen common to all known mouse leukemia viruses (MLV), was used to detect MLV antigens in lymphomas induced in newborn-1-week-old C57BL/6 mice by 3-methylcholanthrene (MC), urethan or diethylnitrosamine (DENA). Extracts of the lymphomas, or of liver and spleen from lymphoma-bearing mice, usually contained MLV complement-fixing antigen. Most DENA-induced tumors were hepatomas or lung adenomas, with a shorter latent period than the lymphomas; none of the extracts of the liver or lung tumors showed MLV antigens. Complement-fixing MLV antigen was also found in low titers, in liver and spleen extracts from a small proportion of vehicle-treated controls or treated mice which did not develop lymphomas. Cell-free extracts of all MC-induced lymphomas with antigen titers of 1:8 or more, and 1/4 tumors with titers of 1:2-1:4, induced leukemia in newborn mice. Some MC-treated mice developed antibodies to MLV before the development of overt lymphoma. It is suggested that unmasking of a latent MLV is an indigenous actuating cause of these lymphomas.

70-409 ALPHA-NAPHTHOFILAVONE: AN INHIBITOR OF HYDROCARBON CYTOTOXICITY AND MICROSOMAL HYDROXYLASE. (E.) Diamond, L. (Wistar Inst., Philadelphia, Pa.) and H. V. Gelboin. Science 166(3908):1023-1025, 1969.

In hamster embryo cell cultures exposed to 3,4-benzpyrene (BP; 0.06 μ g/ml), addition of α -naphthoflavone (ANF; 0.1 or 1.0 μ g/ml; before, simultaneously with or after the addition of ³H-labeled BP) inhibited both the metabolism of BP to water-soluble derivatives and the binding of BP to cellular components (by 70% and over 95%, resp., at 1.0 μ g/ml). ANF had a similar effect

on the metabolism of 7,12-dimethylbenzanthracene (DMBA; 0.1 µg/ml). ANF (5 µg/ml) did not prevent the uptake of BP (1 µg/ml) by the cells. The cytotoxic effects of DMBA and (to a lesser extent) BP were inhibited by ANF. ANF also inhibited aryl hydrocarbon hydroxylase (AHH) activity in homogenates of 1,2-benzanthracene (BA)-induced hamster cells, and in liver microsomes from rats previously treated with BA or 3-methylcholanthrene, but had no effect on AHH activity in control microsome preparations.

70-410 LUNG TUMOR RESPONSE IN STRAIN A MICE AS A QUANTITATIVE BIOASSAY OF CARCINOGENIC ACTIVITY OF SOME CARBAMATES AND AZIRIDINES. (E.) Shimkin, M. B. (U. California Sch. Med., La Jolla, Calif.), R. Wieder, M. McDonough, L. Fishbein and D. Swern. Cancer Res. 29(12):2184-2190, 1969.

Male A/He mice (7-9 wk. old) were treated i.p. for 4 weeks (3 inj./week) with 21 carbamates and 8 aziridines (max. 5.0 and 0.5 mg/inj., total 60 and 6.0 mg, resp.); the lung tumor response was studied 20 wk. after the end of treatment. As a group, the aziridines were more active carcinogenic than the carbamates; 4/8 were definitely carcinogenic and 2/8 had borderline activity. The most active aziridine (3,4-dichlorophenyl-N-carbamoyl-aziridine) was more than 20 times more active than urethan (U); on a molar dosage basis. The most active carbamate was U; 3 other ethyl carbamates (with N-hydroxy-, N-cyanoacetyl- and N-acetyl groups) were nearly as active as U. Two other carbamates had lesser carcinogenic activity, 2 had borderline activity and 13 were inactive.

70-411 PULMONARY TUMORS IN GERMFREE MICE: INDUCTION WITH URETHAN. (E.) Burstein, N. A. (Massachusetts Gen. Hosp., Boston), K. R. McIntire and A. C. Allison. J. Nat. Cancer Inst. 44(1):211-214, 1970.

Germfree and conventional BALB/c mice (6-9-weeks-old) were inj. once with urethan (20 mg i.p.), resulting in fewer subsequent lung tumors in the germfree group (9/17, as compared to 17/20). All conventional BALB/c mice were naturally infected with one or more of 12 common mouse viruses, while only 2 of the germfree BALB/c mice evinced serum antiviral antibody. Urethan oncogenesis as not associated with serologic activity against any single virus.

0-412 A REPLICATION TECHNIQUE FOR THE IDENTIFICATION OF ASBESTOS FIBRES IN MESOTHELIOMAS. (E.) Henderson, W. J. (Welsh Sch. Med., Cardiff, Wales), J. Harse and K. Griffiths. Europ. J. Cancer 5(6):621-624, 1969.

Using a replication technique which either applied or extracted foreign material, asbestos

fibers with features characteristic of crocidolite were visualized by electron microscopy in mesotheliomas from 3 patients.

70-413 TOBACCO SMOKE TOXICITY: LOSS OF HUMAN ORAL LEUKOCYTE FUNCTION AND FLUID-CELL METABOLISM. (E.) Eichel, B. (Sci. Resources Found., Watertown, Mass.) and H. A. Shalrik. Science 166(3911):1424-1428, 1969.

Oral fluid cells were studied before and after the smoking of 1 cigarette from 86 smokers and non-smokers. Before-smoking cell samples from both groups contained normally active leukocytes (inflammatory cells). After 1 cigarette was smoked, the phagocytic activity and motility of these cells was markedly reduced or disappeared. Pre-smoking oral fluid cells showed measurable (sometimes marked) levels of aerobic endogenous and glucose-dependent oxygen consumption and anaerobic glycolysis, which were inhibited in most subjects by smoking 1 cigarette. Studies using various types of filters showed that these toxic effects were caused mainly by the gaseous phase of the smoke, not the particulate fraction. The oral fluid cells obtained before and after smoking were used as an *in vitro* test system, providing a sensitive bioassay to study the *in vivo* effects of smoking.

70-414 ADAPTED DEVELOPMENT OF A CLONE OF DUNALIELLA BIOCULATA TO THE GASEOUS PHASE OF CIGARETTE SMOKE, AND ITS BEHAVIOR IN THE PRESENCE OF 4-NITROQUINOLINE-N-OXIDE AND 4-NITROQUINALDINE-N-OXIDE. (Fr.) Izard, C. (S.E.I.T.A., Paris) and D. Valadaud. C. R. Acad. Sci. [D] Paris 269(1):55-58, 1969.

A clone of Dunaliella bioculata, grown in Miquel sea-water medium containing 0.250 ml soln. of the gaseous phase of cigarette smoke per 10 ml medium showed significant resistance to the effects of the contaminant by the thirteenth passage, continuing to become increasingly resistant through the twenty-seventh. At the time of the thirteenth through nineteenth passages, it also showed progressively increasing resistance to the effects of 4-nitroquinoline-N-oxide (NNO) and 4-nitroquinaldine-N-oxide, followed by stabilization of this phenomenon through the twenty-third passage, its reversal on the twenty-fourth, and the development of a very high degree of susceptibility by the twenty-seventh passage. Correlative studies on normal clones showed that cysteine was capable of blocking the effects of the cigarette-smoke contaminant completely, while competing significantly with NNO. Tryptophan showed a very slight protective effect against the cigarette-smoke contaminant; none, against NNO. It is concluded that the phenomena observed probably resulted from mutation, followed by a selection process.

70-415 DEMONSTRATION OF DELAYED HYPERSENSITIVITY TO SOLUBLE ANTIGENS OF CHEMICALLY INDUCED TUMORS BY INHIBITION OF MACROPHAGE MIGRATION. (E.) Bloom, B. R. (Albert Einstein Coll. Med., New York, N. Y.), B. Bennett, H. F. Oettgen, E. P. McLean and L. J. Old. Proc. Nat. Acad. Sci. USA 64(4):1176-1180, 1969.

The migration of peritoneal cells of sensitized guinea pigs (syngeneic strain 13) was specifically inhibited by the corresponding soluble antigen of chemically induced tumors (3-methylcholanthrene and 7,12-dimethylbenzanthracene). The degree of inhibition was dose dependent within 5-20 vol. per cent of antigen. There was no cross-reactivity as non-corresponding antigen failed to inhibit migration and caused no release of migration inhibitory factor from lymph node cells. This technic may serve as an *in vitro* assay for transplantation antigens of chemically-induced tumors.

70-416 THE EFFECT OF PINEALECTOMY ON CHEMICALLY INDUCED CANCERIZATION OF THE LIVER IN THE RAT. (Fr.) Lacassagne, A. (Inst. Radium, Paris), A. Chamorro, L. Hurst and N. B. Giao. C. R. Acad. Sci. [D.] (Paris) 269(11):1043-1046, 1969.

Ten adult, male Wistar rats were put on a protein- and riboflavin-impooverished diet, beginning 2 mo. after pinealectomy. The feed of 4 of the animals contained 4-dimethylaminoazobenzene (DAB = 0.6 g/kg/day x 135-295, prior to sacrifice); the feed of 3 contained 2-acetylaminofluorene (AAF = 0.3 g/kg/day x 85-183, prior to sacrifice); 3 were maintained as controls, with 1/3 dying spontaneously after 89 days and 2/3 sacrificed, after 190 and 216 days, resp. In addition, 2 adult, male rats of the same strain were fed a normal diet with diethylnitrosamine in the drinking water (DENA = 50 mg/l x 193 and 194 days, resp., prior to sacrifice). As compared to controls in a previous study, pinealectomy exerted no significant effect on carcinogenesis of the liver induced by AAF or DENA. However, it afforded complete protection against hepatic cancerization induced by DAB.

70-417 THE CARCINOGENIC ACTIVITY OF SOME 5-NITROFURAN DERIVATIVES IN THE RAT. (E.) Morris, J. E. (State Univ. Coll., Brockport, N. Y.), J. M. Price, J. J. Lalich and R. J. Stein. Cancer Res. 29(12):2145-2156, 1969.

In female Holtzman rats fed several 5-nitrofuran derivatives (0.1-0.3% in the diet for up to 44.5 weeks), formic acid 2-(4-[5-nitro-2-furyl]-2-thiazolyl)hydrazide induced tumors of the mammary gland (benign or malignant), kidney (adenomas or adenocarcinomas), intestine (adenocarcinomas) and external auditory canal (carcinomas). The only tumors induced by 5-nitro-2-furaldehyde semicarbazone were histologically

benign mammary tumors. Multiple squamous papillomas of the non-glandular forestomach were seen in rats fed acetone 4-[5-nitro-2-furyl]-2-thiazolylhydrazone. Two other 5-nitrofurans (5-nitro-2-furanmethandiol and 1-([5-nitro-furfurylidene]amino)hydantoin) and 5,5-diphenylhydantoin were inactive. Admin. of N-(2-fluorenyl)acetamide (0.03% in the diet) induced benign mammary tumors and carcinomas of the external auditory canal. Since 2 of these 5-nitrofurans were not carcinogenic, it is suggested that the carcinogenic activities of the other 3 agents might be attributable to the effects of the hydrazine or thiazole moieties.

70-418 EXPERIMENTAL STUDY OF THE EFFECTS OF SEVERAL CARCINOGENS ON TROUT LIVER. (It.) Codegone, M. L. (Inst. Path. Anat., Turin, Italy), A. Provana, P. Ghittino and G. Palestro. Cancro 21(5):469-476, 1968.

Mixed groups of rainbow and brown trout received o-aminoazotoluene (AAT = 800 ppm), dimethylnitrosamine (DMN = 800 ppm), or crystalline aflatoxin B₁ (AFT = 0.008 ppm) in fresh beef liver, fed daily x 18-22 mo. in quantities approximating 5% of the live body wt. Prior to mixing with the liver, the agents were suspended in olive oil and mixed with carboxymethylcellulose. Five rainbow and 5 brown trout from each group were sacrificed every 2 mo., and the livers were subjected to macroscopic and histologic study. Among controls receiving the vehicle alone, 0/100 developed hepatomas and 0/100 showed any evidence of liver cell damage and regeneration. Comparable tabulations for fish treated with AAT were 2/100 and 27/100, resp.; for those treated with DMN, they were 0/100 and 0/100, resp.; for those treated with AFT, they were 2/100 and 6/100, resp. Only rainbow trout were affected by the carcinogens, in either way. It is suggested that the low incidence of cancerization may have been due to some protective or carcinogen-inactivating effect exerted by the vehicle or some change which occurred in the substrate during the course of preparing and storing the material.

70-419 CARCINOGENICITY OF HALO-ETHERS. (E.) Van Duuren, B. L. (New York U. Med. Ctr. Inst. Environ. Med. N. Y.), A. Sivak, B. M. Goldschmidt, C. Katz and S. Melchionne. J. Nat. Cancer Inst. 43(2):481-486, 1969.

Applications of bis(chloromethyl)ether (BCME; 2 mg in benzene) induced papillomas in 13/20 mice. Progression of the tumors to squamous cell carcinomas was seen in 12/13 by day 320. When BCME was used as an initiator in a 2-stage skin carcinogenesis test, papillomas developed in 5/20 mice; 2/5 showed progression of the papillomas to carcinomas, and 1 developed lung metastases. The first tumors appeared in 76 days. In rats, inj. of BCME (3 mg/week x 114 days, then 1

mg/week x 186 days) induced fibrosarcomas in 5/20 animals; the first tumor was confirmed 245 days after the initial inj. Chloromethyl methyl ether (CMME) was not carcinogenic for mouse skin, but was a good initiator in the 2-stage skin carcinogenesis test. CMME initiating doses of 1000 and 100 µg, with phorbol ester as the promoter, induced papillomas in 5/20 and 7/20 animals, resp.; progression to carcinomas was seen in 1/20 and 4/20, resp. The latent periods were 140 and 259 days, resp. Inj. of CMME (same doses as BCME) induced a fibrosarcoma in 1/20 rats. Octachlorodi-n-propyl ether, α,α-dichloromethyl methyl ether and monochloroacetaldehyde diethyl acetal were inactive.

70-420 CIRRHOSIS AND CARCINOMA OF THE LIVER IN MALE RATS GIVEN SUBCUTANEOUS CARBON TETRACHLORIDE. (E.) Reuber, M. D. (NCI, Bethesda, Md.) and E. L. Glover. J. Nat. Cancer Inst. 44(2):419-427, 1970.

Male rats of 5 strains were treated s.c. with carbon tetrachloride (2 inj./wk. of 1.3 ml/kg of a 50% soln.) from the age of 12 weeks. In Japanese (J), Osborne-Mendel (O-M) and Wistar rats, av. survival times were 47, 44 and 33 weeks, resp. Liver carcinomas developed in 2/15, 8/13 and 4/12, resp.; all other treated rats showed at least focal hyperplasia of the liver, and 3/15, 4/13 and 7/12, resp., developed hyperplastic nodules. Rats of all 3 strains developed well-differentiated carcinomas, but only the J rats showed poorly differentiated or undifferentiated carcinomas. One J rat developed lung metastases. Black (BL) and Sprague-Dawley (S-D) rats survived an av. of 11 and 13 wk., resp., and died with liver cirrhosis before liver tumors could develop. Cirrhosis was seen in all treated rats, being most severe in the BL and S-D rats. Some J and O-M rats developed hepatic vein thrombosis (2/15 and 2/13, resp.) or cholangiofibrosis (1/15 and 4/13, resp.). Other lesions seen in J and O-M rats included splenic hemangiomas (2/15 and 1/13, resp.), thyroid carcinomas (3/15 and 3/13, resp.) and multicystic kidneys (3/15 and 2/13, resp.); 1 J rat developed s.c. leiomyosarcoma.

70-421 LACK OF CARCINOGENIC EFFECTS OF ISONICOTINIC ACID HYDRAZIDE IN THE SYRIAN GOLDEN HAMSTERS. (E.) Toth, B. (University of Nebraska Coll. Med. Eppley Inst. Res. Cancer, Omaha) and P. Shubik. Tumori 55(3):127-135, 1969.

Isonicotinic acid hydrazide (INH) was given to male and female Syrian golden hamsters (5-6 weeks old), dissolved in their drinking water. Animals given a 0.3% soln. intermittently for 42 weeks had an average daily intake of 13.5 mg; a 2% soln. was given for the life-span, females consuming an av. of 20 mg/day, males 19 mg; a 1% soln. was also given for the life-span of

some animals, consumption averaging 14.7 mg for females, and 17.4 mg for males. Treatment with INH, especially the 0.3% soln., shortened the survival of the hamsters and reduced their wt. No carcinogenic effect was observed.

70-422 INDUCTION OF SARCOMA IN MICE BY A NEW CARCINOGEN, 4-NITROQUINOLINE. (E.) Mori, K., M. Kondo (Showa U. Sch. Med., Tokyo), M. Tamura, H. Ichimura and A. Ohta. Gann 60(6):663-664, 1969.

Female ICR mice (5 weeks old) were treated with 11 s.c. inj. of 4-nitroquinoline (NQ; total 34 mg). After 170-330 days of observation, 12/21 evaluable NQ-treated mice (57.1%) developed s.c. sarcomas; in addition, NQ also induced 3 carcinomas and 7 adenomas of the lung and 4 ovarian cysts. No tumors were seen in vehicle-treated controls.

70-423 INHIBITORY EFFECT OF L-ASCORBATE ON TUMOR FORMATION IN URINARY BLADDERS IMPLANTED WITH 3-HYDROXYANTHRANILIC ACID. (E.) Pipkin, G. E. (Tulane U. Sch. Med., New Orleans, La.), J. U. Schlegel, R. Nishimura and G. N. Schultz. Proc. Soc. Exp. Biol. Med. 131(2):522-524, 1969.

Cholesterol pellets containing 3-hydroxyanthranilic acid (HOA) were implanted into the bladders of 60-120-day-old female Swiss mice, some of which were also treated with ascorbic acid (AA; 250 mg/100 ml) in the drinking water. Controls were untreated or AA-treated mice bearing HOA-free cholesterol implants. The 40-week survival rates in all treated and control groups were about the same. In the 40-week survivors, bladder tumors in mice treated with HOA alone and + AA were 9/46 and 3/37 mice, resp. (8/9 and 2/3 tumors, resp., were malignant), compared to 5/49 and 3/23 in untreated and AA-treated controls, resp. (2/5 and 2/3 tumors, resp., were malignant). It is concluded that AA inhibited the anticipated carcinogenic action of HOA, possibly by preventing the formation of its carcinogenic oxidation product(s) in the urine.

70-424 INFLUENCE OF HORMONES ON N-2-FLUORENYLDIACETAMIDE-INDUCED HYPERPLASTIC HEPATIC NODULES IN RATS. (E.) Reuber, M. D. (NCI, Bethesda, Md.). J. Nat. Cancer Inst. 43(2):445-451, 1969.

Inbred male 12-week-old A x C rats were fed a diet containing 0.025% N-2-fluorenyldiacetamide in 4-week periods followed by 1 week on the basal diet until the carcinogen was admin. for 16 weeks. Hyperplastic nodules were seen in 19/23 rats sacrificed 23 weeks after the start of the experiment, at which time the hormonal status was altered in some groups of animals. Carcinoma of the liver developed in 10/12 intact

rats. Hypophysectomy was most effective in preventing carcinoma (3/12 rats had small carcinomas): and adrenalectomy plus castration was more effective than castration alone or thyroidectomy in reducing incidence. Almost all adrenalectomized animals with or without exogenous cortisone or deoxycorticosterone and the castrated rats admin. testosterone or diethylstilbestrol developed large carcinomas. The carcinomas grew on transplantation in isologous hosts. It is suggested that progression of hyperplastic nodules depends on the hormones of the host.

70-425 PRELIMINARY STUDIES ON THE IN VITRO CARCINOGENESIS OF RAT THYMUS CELLS BY N-METHYL-N'-NITRO-N-NITROSOGUANIDINE. (E.) Takaki, R. (Kyushu U., Fukuoka, Japan), M. Takii and T. Ikegami. Gann 60(6):661-662, 1969.

Thymus cell cultures derived from 4-day-old inbred Wistar-King A (WKA) rats were exposed for 6 days to N-methyl-N'-nitro-N-nitrosoguanidine (NG; 10 µg/ml). The treated cells recovered from the cytotoxic effects of NG and began to grow several wk. after the end of NG exposure. Contact inhibition was lost after about 2 mo. of cultivation, but cells from 69-day cultures induced no tumors after s.c. inoc. into 3-week-old WKA rats. Signs of transformation became evident after 5 mo. Cells obtained from 305-day cultures induced pleomorphic sarcomas (after latent periods of about 2 mo.) in 3/9 newborn WKA rats after s.c. inoc. Control cells from 394-day cultures did not induce s.c. tumors.

70-426 THE PRODUCTION OF HEMANGIOENDOTHELIAL-SARCOMA IN RATS BY FEEDING 5-ACETAMIDO-3-(5-NITRO-2-FURYL)-6H-1,2,4-OXADIAZINE. (E.) Ertürk, E. (U. Wisconsin Med. Sch., Madison), S. M. Cohen, J. M. Price, A. M. Von Esch, A. J. Croveti and G. T. Bryan. Cancer Res. 29(12): 2212-2218, 1969.

Of 35 weanling female Sprague-Dawley rats fed 5-acetamido-3-(5-nitro-2-furyl)-6H-1,2,4-oxadiazine for 37 weeks (0.189% in diet for 21 weeks, then 0.15%), 32/35 survived 28 weeks or more. Hemangioendothelial sarcomas of 1 or more sites developed in 32/32 of the 28-week survivors (liver in 31/32, mesentery in 30/32, lung in 5/32). Other tumors included 9 alveolar carcinomas and 1 benign fibroadenoma of the mammary gland.

70-427 PATHOGENESIS, HISTOLOGY, AND TRANSPLANTABILITY OF URINARY BLADDER CARCINOMAS INDUCED IN ALBINO RATS BY ORAL ADMINISTRATION OF N-[4-(5-NITRO-2-FURYL)-2-THIAZOLYL]FORMAMIDE. (E.) Ertürk, E. (U. Wisconsin Med. Sch., Madison), S. M. Cohen, J. M. Price and G. T. Bryan. Cancer Res. 29(12): 2219-2228, 1969.

In male Sprague-Dawley rats fed N-[4-(5-nitro-2-furyl)-2-thiazolyl]formamide (NFTF; 0.188% in the diet) for 26 or 46 weeks, all rats surviving 24 weeks or more developed grossly visible transitional or squamous cell carcinomas of the bladder. Severe hyperplasia of the renal pelvis was seen in 19/35 and carcinomas of the renal pelvis (invading the kidney) in 4/35 of the 24-week survivors. In female Sprague-Dawley rats fed NFTF (same doses), all animals surviving 9 weeks developed bladder carcinomas. Hyperplasia of the transitional epithelium was seen in rats sacrificed after 3 wk. of NFTF admin. At 8 weeks, squamous metaplasia and increased mucosal mitotic activity developed. Microscopic papillary or sessile transitional cell carcinomas were found within 9 wk. and small, grossly detectable tumors appeared after 12 weeks. NFTF-induced bladder carcinomas from male Sprague-Dawley rats were transplantable s.c. into weanling female Sprague-Dawley rats. Tumor transplantability was best when squamous metaplasia was present.

70-428 CARCINOMAS OF THE GLANDULAR STOMACH AND OTHER ORGANS OF RATS BY 4-HYDROXY-AMINOQUINOLINE 1-OXIDE HYDROCHLORIDE. (E.) Mori, K., A. Ohta (Tokyo Inst. Tech., Tokyo), T. Murakami, M. Tamura, M. Kondo and H. Ichimura. Gann 60(6):627-630, 1969.

Female Buffalo rats were treated with 4-hydroxy-aminoquinoline-1-oxide HCl (1 or 2 mg p.o. every 3 wk., total 30 mg) and observed for up to 610 days. Among the rats surviving over 287 days from the beginning of the experiment, 7/28 developed glandular stomach tumors: 2 advanced adenocarcinomas (7.1%), 1 signet ring-cell carcinoma with submucosal invasion (3.6%) and 4 mucosal carcinomas (14.3%). Mammary tumors developed in 6/28 evaluable rats (including 2/7 rats with stomach tumors), thymomas in 5/28, carcinomas of the lung and intestine in 2/28 and 1/28, resp., and a uterine sarcoma in 1/28. No tumors were seen in vehicle-treated controls.

70-429 ORIGIN AND BEHAVIOR OF CLEAR-CELL TUMORS OF THE THYROID IN THE RAT. (Fr.) Stoll, R. (Bergonie Found. Biol. Lab., Bordeaux, France), R. Maraud and N. Faucounau. Europ. J. Cancer 5(6):543-551, 1969.

When sacrificed 4-17 mo. after treatment was terminated, inbred, male Wistar rats receiving propylthiouracil (PTU) in their drinking water for 1-3 mo. prior to reaching age 9 mo. showed only occasional, very small, clear-cell (para-follicular) thyroid adenomas, which exhibited no significant mitotic activity. Animals which also received 30 µC ¹³¹I, s.c., at the end of the treatment period frequently developed much larger clear-cell adenomas in which mitotic activity was significantly greater than that of the ambient vesicular tissue from which they appeared to develop, although actual cancerization

was not demonstrated, due to the shortness of the maximal, overall experimental period. Both the mean size of these tumors and the frequency with which they appeared were related directly to the length of the PTU treatment period, while the mean latency period was also significantly shorter in animals receiving PTU for 3 mo. In a final group of animals, previously treated with PTU and ^{131}I , as above, admin. of pituitary thyroid-stimulating hormone (TSH) for 3 consecutive days, terminating 24 hours before sacrifice, had no discernible effect on tumor incidence, tumor size, or the mitotic rate of tumor tissue, although the mitotic rate of ambient vesicular tissue was increased significantly. It is concluded that TSH does not play a significant role in the production of this type of thyroid tumor.

70-430 CHEMICAL CARCINOGENESIS AND FREE RADICALS. (Fr.) Duchesne, J. (U. Liege Inst. Phys., Belgium), Y. Lion and A. Van De Vorst. *C. R. Acad. Sci. [D] (Paris)* 269(16):1562-1563, 1969.

In 7-mo.-old, pure-bred J0 white rats subjected to spectrography, normal liver tissue gives back an electronic paramagnetic resonance signal situated at $g = 2.005$, with an intensity of approx. 15 oersteds and with individual variations not exceeding 15%. In rats fed a combination of boiled rice and raw carrot (10 g/day) containing mineral oil (2%) plus p-dimethyl-iminoazobenzene (6 mg/day) or 2-acetylaminofluorene (4 mg/day), signals recorded at ordinary temperatures on the forty-third day of treatment were 0.6 and 1.6 times this normal, base intensity, resp. At 77 days, they were 0.5 and 0.7 times the base rate, decreasing, with some fluctuation at varying time intervals, to reach zero on day 210 and day 273, resp. No readings were made prior to day 43, although significant indices of change can be presumed to have occurred earlier, in contrast to the minimum of 1 mo. required to demonstrate cancerization macroscopically. The possibility of using this technique as an early detector of hepatic cancer is suggested. Note is made that a signal which has been reported previously as following the onset of cancerization, and which is characterized by a spectroscopic decomposition factor of $g = 2.035$, has also been demonstrated as a secondary phenomenon in the presence of normal hepatic tissue, and occurs too irregularly, in any case, to be considered a reliable test.

70-431 CARCINOGEN-INDUCED TUMORS OF THE THYMUS. III. RESTORATION OF NEONATALLY THYMECTOMIZED MICE WITH THYMOMAS IN CELL-IMPERMEABLE CHAMBERS. (E.) Stutman, O. (U. Minnesota Med. Sch., Minneapolis), E. J. Yunis and R. A. Good. *J. Nat. Cancer Inst.* 43(2): 9-508, 1969.

Implantations (i.p.) of diffusion chambers containing nonlymphoid functional thymomas showed

capacity to restore 20-day-old neonatally thymectomized C3Hf/Bi mice. Implantation of empty chambers, chambers containing a C3H/Bi s.c. sarcoma or chambers containing each of 9 different other tumors did not restore any of the thymectomized hosts. The percent of restored animals was 41-65% for thymomas grafted within diffusion chambers with 0.22 pore size filters; the restorative effect decreased when tumors were grafted within chambers with 0.10 μ pore size filters. Comparable effects were seen with thymus from 20-day-old donors within the diffusion chambers. Immunological functions of the restored animals were comparable to those of normal controls. Amyloidosis of the spleen was seen in 4/32 and 1/19 animals treated with thymoma A and C3H#1, resp.; and in 2/26 animals grafted with thymoma C3H#2, at autopsy at 200 days. None of the animals grafted with thymus showed amyloidosis at 200 days.

70-432 STUDIES ON CHEMICAL CARCINOGENS. XI. METABOLISM OF TRITIATED CARCINOGENIC 4-NITROQUINOLINE 1-OXIDE AND DISTRIBUTION OF ITS METABOLITES IN MOUSE. (E.) Kawazoe, Y. (Nat. Cancer Ctr. Res. Inst., Tokyo), N. Uehara, M. Araki and M. Tamura. *Gann* 60(6):617-626, 1969.

The distribution of ^3H -labeled 4-nitroquinoline 1-oxide (NQO; 1.0 mg s.c.) and its breakdown into 4-hydroxyaminoquinoline, 4-hydroxyaminoquinoline-1-oxide (HAQO), 4-aminoquinoline and 4-aminoquinoline-1-oxide, was studied in female ddN mice. At 30 min. or 2 hr. after inj., label uptake by the lungs was greater than uptake by the liver or spleen. This high level of label accumulation by the lungs was transient; at 5 hr., less label was found in the lungs than in the blood. The conc. of NQO was much lower than that of HAQO in any tissue studied, except the blood and the inj. site. Splenic levels of label were consistently lower than blood levels at all times from 30 min.-7 days after NQO admin. The liver contained non-carcinogenic metabolites almost exclusively, with only traces of the carcinogenic compounds (NQO and HAQO).

70-433 METABOLISM OF THE CARCINOGEN N-HYDROXY-N-2-FLUORENYLACETAMIDE IN GERM-FREE RATS. (E.) Weisburger, J. H. (NIH, Bethesda, Md.), P. H. Grantham, R. E. Horton and E. K. Weisburger. *Biochem. Pharmacol.* 19(1):151-162, 1970.

Male, germ-free or conventional Fischer rats were inj. i.p. with ^{14}C -labeled N-hydroxy-N-2-fluorenylacetamide (N-OH-FAA; 10 mg/kg). More radioactivity was seen in the liver and less in the plasma in the germ-free groups than in controls. Urinary excretion of total metabolites was similar in the 2 groups but the germ-free rats excreted much larger amounts of the glucuronic acid conjugates of N-OH-FAA than conventional rats. The ceca of the axenic rats contained more radioactivity, and the major fraction of

the metabolites consisted of sulfuric and glucuronic acid conjugates. Fecal radioactivity was similar in both groups, but the metabolites in the germ-free animals were largely conjugated. In the conventional rats, fecal and cecal metabolites were mostly of the free, unconjugated type. Cecal β -glucuronidase in germ-free rats had an optimum pH of 5, compared to pH 6 in conventional animals. N-OH-FAA, inj. into the cecum was readily resorbed and metabolized.

70-434 METABOLISM OF THE CARCINOGEN N-2-FLUORENYLACETAMIDE IN GERM-FREE AND CONVENTIONAL RATS. (E.) Grantham, P. H. (NIH, Bethesda, Md.), R. E. Horton, E. K. Weisburger and J. H. Weisburger. Biochem. Pharmacol. 19(1):163-171, 1970.

Germ-free and conventional male Fischer rats were inj. i.p. with ^{14}C -labeled N-2-fluorenylacetamide (FAA; 50 mg/kg). Levels of radioactivity from FAA in germ-free animals were the same in the blood, and only slightly less in the urine after 48 hr., as compared to controls. The urine of the germ-free animals contained more of the 7-hydroxylated derivative and less of the 5-hydroxy derivative than the urine of controls; the controls excreted more of the dose in the feces than the germ-free rats. After 24 hr., the germ-free rats showed 18% of the dose in the cecum, compared to 7% in the controls. Almost all of the FAA metabolites in the germ-free animals were conjugated with glucuronic or sulfuric acid, but were mostly free and unconjugated in the conventional animals. It is suggested that the FAA conjugates undergo additional metabolism after being converted to free compounds by the intestinal flora of conventional animals.

See also abstract nos.: 351,352,534,537,542,544,545

VIRAL CARCINOGENESIS

70-435 STUDIES ON MOUSE LEUKEMIA VIRUSES. 1. ISOLATION AND CHARACTERIZATION OF A GROUP-SPECIFIC ANTIGEN. (E.) Schäfer, W. (Max Planck Inst. Virus Res., Tübingen, Germany), F. A. Anderer, H. Bauer and L. Pister. Virology 38(3):387-394, 1969.

A group-specific antigen in Friend virus was isolated and purified by Tween 80-ether treatment, sucrose gradient centrifugation, and Sephadex G-150 column chromatography. The high purity of the antigenic material was confirmed by analytical ultracentrifugation, electrophoresis, and complement fixation tests using rabbit antiserum against purified Rauscher virus treated with sodium dodecyl sulfate. In agar gel diffusion, the antiserum yielded a continuous line with Friend virus antigen, Rauscher virus, Gross virus, and a mouse leukemia virus contained in L cell cultures. The group-specific antigen of Friend virus was a strongly basic protein, with a molecular wt. of approx. 26,000 daltons, and its amino acid composition was analyzed.

70-436 INHIBITION OF FRIEND VIRUS-INDUCED SPLENOmegALY BY AN ASSOCIATED LYMPHATIC LEUKEMIA VIRUS. (E.) Dawson, P. J. (U. Oregon Med. Sch., Portland) and A. H. Fieldsteel. Proc. Soc. Exp. Biol. Med. 132(3):898-915, 1969.

In young adult female BALB/c mice infected with Friend leukemia virus (FLV), 1-21 days after infection with FLV-free lymphatic leukemia virus (LLV; isolated from FLV and always associated with LLV), the development of reticulum cell proliferation in the spleen was retarded, if LLV was inj. 7-21 days before FLV. Best results were seen when the interval between LLV and FLV infection was 21 days. LLV did not affect the development of FLV infection if the interval was 1 day or less. Prior infection with LLV, however, did not inhibit FLV proliferation.

70-437 EFFECT OF FRIEND LEUKEMOGENIC VIRUS ON ANTIBODY-FORMING CELLS TO A BACTERIAL ANTIGEN. (E.) Hirano, S. (Temple U. Sch. Med., Philadelphia, Pa.), W. S. Ceglowski, L. Allen and H. Friedman. J. Nat. Cancer Inst. 6(6):1337-1345, 1969.

Numbers of plaque-forming cells (PFC) were markedly depressed in adult female BALB/c mice immunized with *E. coli* antigen and infected with Friend leukemia virus (FLV) 3, 7, or 14 days before immunization. No significant suppression occurred in animals infected with FLV 1 or 2 days after immunization. Suppression of agglutinin titers to *E. coli* was also seen in animals infected with FLV before immunization. The degree of suppression of the antibody titer was less than that occurring on the cellular level. Infection with

FLV did not affect the number of "background" antibody-forming cells. Marked immunosuppression of induced PFC cells seemed related to degree of splenomegaly.

70-438 TISSUE CULTURE ASSAY FOR MOLONEY LEUKEMIA VIRUS. (E.) Nordenskjöld, B. A. (Karolinska Inst., Stockholm), E. Klein, T. Tachibana and E. M. Fenyo. J. Nat. Cancer Inst. 44(2):403-412, 1970.

In mouse bone marrow cells (the JLS-V9 cell line) infected with Moloney leukemia virus (MLV), a new surface antigen was detected by indirect membrane immunofluorescence and immune adherence to living target cells, using sera from MLV-immunized mice as a reagent. More than 60% of the JLS-V9 cells remained positive in the immunofluorescence test during 6 mo. of repeated testing. The antiviral activity of the mouse serum could be determined by the *in vitro* infectivity test. The time course of antigen expression was studied, using different sources and dilutions of MLV. This method was useful for the assay of MLV infectivity, as well as the *in vivo* leukemogenic and immunogenic activities and the *in vitro* antigen-inducing activity of MLV preparations.

70-439 ELECTRON MICROSCOPIC STUDIES ON THE LOCALIZATION OF ANTIBODIES IN RAT LYMPH NODE CELLS PRODUCING MOLONEY VIRUS. (E.) Oshiro, L. S. (California State Dept. Pub. Health, Berkeley), N. E. Cremer, D. O. N. Taylor and E. H. Lennette. J. Nat. Cancer Inst. 43(5):1109-1118, 1969.

Inbred Osborne-Mendel rats, infected at age 48-72 hr. with Moloney leukemia virus (MLV; preparation RT34), were hyperimmunized at age 2 mo. with apoferritin, and sacrificed 4 days after booster immunization (3-5 wk. after hyperimmunization). Lymphomatous changes were seen in the thymuses of 9/17 MLV-infected rats, but the spleens and lymph nodes were within normal limits. Electron microscopic examination of ferritin-treated frozen lymph node sections revealed ferritin deposition (indicating the presence of apoferritin antibodies) in the cisternae of the endoplasmic reticulum, the Golgi region and the perinuclear spaces of some lymph node cells from both infected and control rats. Antibody-containing cells were more frequent in the lymph nodes from uninfected controls. The presence of budding C-type particles and ferritin within the same cell indicated the production of MLV in cells that were, or had been, producing antibody.

70-440 MIXED CULTURE CYTOPATHOGENICITY: A NEW TEST FOR GROWTH OF MURINE LEUKEMIA VIRUSES IN TISSUE CULTURE. (E.) Klement, V.

(Children's Hosp. Los Angeles, Calif.), W. P. Rowe, J. W. Hartley and W. E. Pugh. Proc. Nat. Acad. Sci. USA 63(3):753-758, 1969.

Leukemia virus infected mouse embryo cell cultures (14-17-day NIH Swiss and BALB/cN mouse embryos), when overlaid with rat tumor cells (Rous-virus induced, XC line of Svoboda et al.) induced a three-stage effect which may serve as a sensitive qualitative and quantitative indicator of rat or mouse leukemia virus: (1) 3-6-hour formation of syncytial areas with four to several dozen nuclei. (2) 2-3 days - appearance of bizarre, giant, vacuolated round cells. (3) 1 week - protection of mouse cell sheet from invasion. This technic has been demonstrated to be more sensitive than the complement fixation (COMUL) or the fluorescent antibody tests. This principle may be applicable to leukemia viruses of other species.

70-441 IMMUNIZATION OF AKR MICE BY CELLS OF A LEUKEMIA INDUCED BY GROSS VIRUS: ABSENCE OF TOLERANCE. (Fr.) Doré, J.-F. (Paul Brousse Hosp., Villejuif, France), E. Ajuria and G. Mathé. C. R. Acad. Sci. D. (Paris) 269(24): 2479-2482, 1969.

As compared to controls which received no pretreatment, 2-mo.-old, female AKR mice which had been immunized by s.c. inj. of the cells of a leukemia (GVL-2) induced in male C57BL/6 mice by Gross virus showed significant prolongation of survival times after i.p. inj. of leukemia K 36 cells, with a corresponding increase of the mean survival time and with 6/24 pretreated animals still surviving after more than 70 days, in contrast to a max. control survival time of 30 days. In a correlative study, similar results were obtained with animals previously immunized by GVL-2, as above, but not with animals previously treated with BCG alone or with BCG + GVL-2. No cytotoxic antibodies could be demonstrated in any of the groups in this correlative study, including animals inoc. with K 36 cells alone, in the absence of pretreatment, and animals receiving GVL-2 cells, alone. However, antibodies reacting against K 36 cells by immune adherence were demonstrated in a control group receiving BCG + GVL-2 simultaneously (but no K 36 cells, subsequently), the group receiving BCG prior to the K 36 cells, and the group receiving GVL-2 prior to the K 36 cells. When previously untreated animals and animals which had previously survived leukemia K 36 were inoc. s.c. with progressively increasing doses of K 36 cells, admin. 1x/ or 2x/week, cytotoxic antibodies were demonstrable in the serum from the eighth inj. on, in a titer equal or superior to 1/32 for K 36 cells, AKR spontaneous leukemia cells, and/or cells derived from the first transplant generation of a leukemia induced in C3H/Jax mice by neonatal inj. or Gross virus Passage A.

70-442 MOUSE LEUKEMIA VIRUS: "SPONTANEOUS" RELEASE BY MOUSE EMBRYO CELLS AFTER

LONG-TERM IN VITRO CULTIVATION. (E.) Aaronson, S. A. (NCI, Bethesda, Md.), J. W. Hartley and G. J. Todaro. Proc. Nat. Acad. Sci. USA 64(11): 87-94, 1969.

Rapid transfer at high cell density of certain tumorigenic lines of BALB/c mouse embryo cells (3T12-4) will cause release of a mouse leukemia virus (viral antigen is first detected by fluorescent antibody at the 25th passage; by complement fixation at over 30 passages). Characteristics of the recovered virus are similar to those of mouse leukemia virus isolated from a high percentage of adult BALB/c mice; good growth in NIH Swiss embryo cells and poor growth in BALB/c embryo cells. The evidence suggests that the viral genome is present in the original embryo cultures.

70-443 INTERFERON AND MURINE LEUKEMIA. VI. EFFECT OF INTERFERON PREPARATIONS ON THE LYMPHOID LEUKEMIA OF AKR MICE. (E.) Gresser, I. (Inst. Cancer Res. Viral Oncol. Lab., Villejuif, France), J. Coppey and C. Bourali. J. Nat. Cancer Inst. 43(5):1083-1089, 1969.

Newborn AKR mice were treated with a highly conc. preparation of mouse brain interferon (controls were untreated, or inj. with "normal" brain extracts) for the first 3 mo. or 1 yr. of life. The 3-mo. interferon treatment significantly reduced the spontaneous leukemia incidence and prolonged the survival time in males, but not in females; the 1-yr. course of interferon significantly inhibited leukemia development in both males and females. Tumors of the salivary glands, attributed to polyoma virus, developed in 3/79 interferon-treated mice and 22/81 mice treated with control brain extracts, but did not develop in the untreated controls. A similar interferon treatment (from birth to age 115 days) increased the survival time in male and female AKR mice neonatally inoc. with extracts of AKR leukemic tissue (in this experiment, the males were orchietomized at age 60 days), but all treated and control mice died with leukemia.

70-444 THE PATHOGENESIS OF AUTOIMMUNITY IN NEW ZEALAND MICE. I. INDUCTION OF ANTINUCLEIC ACID ANTIBODIES BY POLYINOSINIC-POLYCYTIDYLIC ACID. (E.) Steinberg, A. D. (Nat. Inst. Arthritis Metabol. Dis., Bethesda, Md.), S. Baron and N. Talal. Proc. Nat. Acad. Sci. USA 63(4):1102-1107, 1969.

The effects of polyIpolyC following multiple injections in mice (NZB and NZW; F₁ hybrids from NZB female and NZW male) are: The induction of interferon, polyIpolyC antibodies, DNA antibodies and the accelerated development of nephritis (in female B/W mice). Induction of serum interferon concentrations adequate to suppress the C-Type murine leukemia viruses also resulted in an increase in autoimmune diseases resembling human systemic lupus erythematosus. Anti-DNA

formation, both spontaneous and induced, appeared earlier in the female and was shown to be unrelated to hormonal influence. Half the B/W mice have naturally occurring polyIpolyC antibodies, probably due to cross reactions with some other RNA. Efforts to produce antibody to native DNA have been unsuccessful, but the LCM virus (double-stranded RNA) will also accelerate the production of DNA antibodies and nephritis. A proposed mechanism of this disease is a genetic hypersensitivity (especially female) to nucleic acid antigen.

- 70-445 CONCOMITANT LOSS OF SPECIFIC CELL-SURFACE ANTIGEN AND DEMONSTRABLE TYPE-C VIRUS PARTICLES IN LYMPHOMAS INDUCED BY RADIATION LEUKEMIA VIRUS IN RATS. (E.) Ferrer, J. F. (U. Pennsylvania Sch. Vet. Med., Kennett Square) and F. A. Gibbs, Jr. J. Nat. Cancer Inst. 43(6): 1317-1330, 1969.

Abundant type C virus particles were present in the leukemic tissues and plasma of W/FU rats pre-irradiated and inoc. i.p. or s.c. with $10-25 \times 10^7$ viable cells from radiation leukemia virus (Rad LV)-induced tumors from newborn rats. All lymphomas rejected by the adult syngeneic hosts had high AdLV cell-surface antigen concentrations. Antigen concentration was lower in a small number of tumors able to grow in nonirradiated adult hosts. Progressive growth of Rad LV-induced lymphomas in rats preimmunized with the same tumor occurred occasionally. Sublines isolated from these growths were maintained by serial transplantation in nonirradiated adult rats, and were not susceptible to the rejection response of specifically preimmunized rats. They exhibited full resistance to the specific cytotoxicity of RadLV antisera. A complete loss of the RadLV antigen after serial passage in nonirradiated recipients was indicated by absorption experiments. Electron microscopic studies of these sublines showed that virus particles were either absent or very decreased in concentration.

- 70-446 ANTIGENIC EXPRESSION OF A MURINE LYMPHOMA DURING GROWTH IN VITRO. (E.) Cikes, (Karolinska Inst., Stockholm). Nature (London) 5(5233):645-647, 1970.

Lymphoma induced by i.p. inoc. of Moloney virus to newborn (A/Sn x A.CA)F1 mice was explanted and tested for antibody-mediated cytotoxic sensitivity during 5 days in culture. Using an initial concentration of 2×10^5 cells/ml, the cytotoxic sensitivity fell to very low levels 48 hours after seeding, remained low for 24 hours and rose within 48 hr. to a cytotoxic index of 0.90. The cytotoxic sensitivity correlated directly with the population doubling time and the concentration of antigenic receptors on the cell surface.

- 70-447 FELINE LEUKEMIA VIRUS: OCCURRENCE OF VIRAL ANTIGEN IN THE TISSUES OF CATS

WITH LYMPHOSARCOMA AND OTHER DISEASES. (E.) Hardy, W. D., Jr. (Sloan-Kettering Inst. Cancer Res., New York, N.Y.), G. Geering, L. J. Old, E. DeHarven, R. S. Brodey and S. McDonough. Science 166(3908):1019-1021, 1969.

Feline leukemia virus (FLV) antigen was detected in tissues from 28/36 cats with spontaneous or FLV-induced lymphosarcoma, 5/13 cats with infectious peritonitis, and 1/11 clinically normal cats. The apparently normal cat showing FLV antigen was from a household in which 2 other cats had developed lymphosarcoma. FLV antigen was also found in a lymphosarcoma induced in a dog by neonatal FLV infection; tissues from several other dogs (similarly infected with FLV) which did not develop lymphosarcomas, contained no FLV antigen. The presence of FLV antigen was correlated with the occurrence of FLV particles in the specimens examined. No FLV antigen was detected in specimens from cats with other types of tumors or with non-malignant diseases, or in lymphosarcomas or non-lymphomatous tumors of other species (man, dog, cow, goat or pig).

- 70-448 SYNCYTIIUM-FORMING AGENT ISOLATED FROM DOMESTIC CATS. (E.) Riggs, J. L. (California State Dept. Pub. Health, Viral Rickettsial Dis. Lab., Berkeley), L. S. Oshiro, D. O. N. Taylor and E. H. Lennette. Nature (London) 222(5199):1190-1191, 1969.

The characteristic cytopathic effect of the syncytium-forming agent (SFA) was observed, by day 21 of culture, in monolayers of lymph node cells from 8/9 cats with various malignant lymphomas and 2/3 cats with non-malignant diseases. SFA could be passed in established feline cell cultures, but not in chick embryos; it did not cause hemagglutination of cat, guinea pig or chicken RBC. The SFA particles were myxovirus-like, but were morphologically different in several respects from the C type particles often noted in feline lymphomas. SFA was not found in the cultures until most cells had formed syncytia, and was not observed in the original tumor tissues. Both myxovirus-like and C type particles were found in the same lot of cultured cells, isolated from lymphomatous cats carrying the adventitious agent.

- 70-449 TRANS-SPECIES RESCUE OF DEFECTIVE GENOMES OF MURINE SARCOMA VIRUS FROM HAMSTER TUMOR CELLS WITH HELPER FELINE LEUKEMIA VIRUS. (E.) Sarma, P. S. (NCI, Bethesda, Md.), T. Log and R. J. Huebner. Proc. Nat. Acad. Sci. USA 65(1):81-87, 1970.

Cultured hamster tumor cells (containing defective Moloney MSV; Kirsten MSV; Harvey MSV - 2×10^6 cells) and feline leukemia virus ((FeLV) - 10^6 infectious units derived from a cat with naturally occurring lymphosarcoma) were inoculated (IM) in 3 - 5 newborn kittens. When tumors developed,

cell-free 10% extracts ($3 - 8 \times 10^3$ focus-forming units/ml) were cultured in NIH Swiss mouse embryo fibroblasts (MEF) and feline embryo fibroblasts (FEF) and observed for cell transformation. Results of the studies done were: (1) transformation foci were induced in the FEF and not the MEF cultures. (2) 0.5 ml of the pseudotype virus was injected IM into 3 newborn kittens, one of which developed a 2 cm mass resembling a myxosarcoma at the site of inoculation. (3) Excess (3 logs) FeLV was found in the mixed virus culture. (4) The Moloney and Kirsten pseudotype viruses showed a defective virus titration pattern. Addition of FeLV increased the pseudotype virus titer. (5) Rabbit anti-serum to FeLV reduced the focus-forming titer 95-98%; antiserum to the defective virus had no effect. (6) FEF cultures chronically infected with FeLV were resistant to all strains of pseudotype virus (10^3 focus-forming units).

70-450 COMPLEMENTARY NUCLEAR RNA'S OF MURINE SARCOMA-LEUKEMIA VIRUS COMPLEX IN TRANSFORMED CELLS. (E.) Biswal, N. (Baylor Coll. Med., Houston, Tex.) and M. Benyesh-Melnick. Proc. Nat. Acad. Sci. USA 64(4):1372-1379, 1969.

Subunits (37S) of MSV-MLV RNA (69S), produced by heating to 95°C for two minutes, hybridized with two heterogeneous species of nuclear RNA from cells (78A1) transformed by and chronically infected with the virus complex. One species of nuclear RNA, 31 - 36S, contained only single-stranded molecules and annealed more efficiently (21.6%) with the viral 37S subunits than did the other 18 - 22S species (19.7%) which contained mostly double-stranded molecules. There was minimal hybridization between the viral RNA and cytoplasmic RNA or RNA from normal cells (RE-2).

70-451 SYNTHETIC DOUBLE-STRANDED RNA: INHIBITORY EFFECT ON MURINE LEUKAEMIA AND SARCOMA VIRUSES IN CELL CULTURES. (E.) Rhim, J. S. (NIH, Bethesda, Md.), C. Greenawalt and R. J. Huebner. Nature (London) 222(5199): 1166-1168, 1969.

The effects of polyinosinic:polycytidylic acid (poly-I:poly-C) on virus replication and cellular transformation were studied in mouse embryo (ME) cells infected with Moloney sarcoma virus (M-MSV), the M-MSV(FL) pseudotype virus, or Friend leukemia virus (FLV). The transforming ability of both M-MSV and M-MSV(FL) was significantly inhibited by poly-I:poly-C. Significant inhibition was seen at 50 µg/ml and max. inhibition at 100 µg/ml; higher conc. of poly-I:poly-C were toxic to the cells. Poly-I:poly-C also inhibited FLV growth in ME cells. The inhibitory effect was enhanced more than 10-fold when neomycin (300 µg/ml) was added to the poly-I:poly-C (100 µg/ml) preparation.

70-452 PHYSICAL PROPERTIES OF COMPETENT AND DEFECTIVE STATES OF A MURINE SARCOMA

(MOLONEY) VIRUS. (E.) O'Connor, T. (NCI, Bethesda, Md.) and P. J. Fischinger. J. Nat. Cancer Inst. 43(2):487-497, 1969.

"Competent" Moloney sarcoma virus (C-MSV), which formed foci on 3T3 mouse cells without coinfection by endogenous Moloney leukemia virus (E-MLV), was found in MSV stocks, in addition to defective MSV (D-MSV) and MLV. Treatment by ultrasonic vibration caused selective inactivation of C-MSV, and minimally affected D-MSV and MLV. C-MSV was separated from D-MSV by differential centrifugation and in sedimentation on sucrose gradients. D-MSV had a lower sedimentation coefficient. C-MSV was found in viral pellets prepared by high-speed centrifugation from stocks of D-MSV and E-MLV. Examination indicated the formation of C-MSV during high-speed pellet formation and during the final freezing of viral preparation. Filtration of dilutions of crude MSV gave successively enriched D-MSV preparation. The authors conclude that C-MSV consists of an interval aggregation of MSV and MLV, that can form during laboratory procedures.

70-453 ROUS SARCOMAS IN MICE: THE CHROMOSOMAL PROGRESSION IN PRIMARY TUMOURS. (E.) Mark, J. (U. Lund Inst. Genet., Sweden). Europ. J. Cancer 5(4):307-315, 1969.

Changes in chromosomal pattern during tumor growth were studied in 11 primary sarcomas induced by Rous sarcoma virus (Schmidt-Ruppin strain) in newborn inbred CBA mice. Five originally diploid tumors underwent heteroploid transformation. The new stemline was often traced to a pre-existing heteroploid subline, which in turn was sometimes traceable to a small fraction of variant cells. The originally heteroploid sarcomas often showed further chromosomal rearrangements during growth, but did not show changes in the original stemline category. Major changes in the chromosomal progression pattern were correlated to tumor histology (fibrosarcomas, spindle cell sarcomas and anaplastic sarcomas), but no clear correlation was seen between chromosomal progression and changes in the tumor growth rate.

70-454 DEVELOPMENTAL KINETICS OF ROUS SARCOMA VIRUS (SCHMIDT-RUPPIN STRAIN). ESTIMATION OF THE TIME OF INCORPORATION OF AGRININE INTO VIRAL PROTEINS. AN AUTORADIOGRAPHIC AND ELECTRON MICROSCOPIC STUDY. (Fr.) Michelson-Fiske, S. (Coll. France Lab. Exp. Med., Paris), F. Haguénau and G. F. Rabotti. C. R. Acad. Sci. [D] (Paris) 269(24):2475-2478, 1969.

ELB chick embryo fibroblasts infected with purified Rous sarcoma virus were cultured for 15 hours in Eagle's medium without arginine and incubated with ^3H -L-arginine. After 1-4 hours the cells were subjected to high resolution autoradiographic study. The viral particles

were clearly labeled by the end of the first hour, with labeling maintained at essentially the same level during the 3 hours following. When the infected fibroblasts were incubated with ^3H -uridine, the rates of incorporation of uridine into viral RNA and of arginine into viral proteins were essentially parallel during the first 2 hours, suggesting that the rate of synthesis of RNA and that of the arginine-incorporating proteins were highly comparable, up to this time. After the second hour, however, the incorporation of arginine plateaued, while incorporation of uridine continued to increase markedly, suggesting that the initial conc. of the 2 precursors may have been different or that the synthesis of viral proteins (or at least some of them) proceeds more rapidly than synthesis of viral RNA, although the rate of utilization of these viral proteins in the viral particle as a whole parallels the rate of RNA synthesis.

70-455 HYBRIDIZATION OF RNA FROM ROUS SARCOMA VIRUS WITH CELLULAR AND VIRAL DNA'S. (E.) Yoshikawa-Fukada, M. (Carnegie Inst. Washington, Baltimore, Md.) and J. D. Ebert. Proc. Nat. Acad. Sci. USA 64(3):870-877, 1969.

Homologous base sequences were investigated by hybridization of ^{32}P -labeled Rous sarcoma virus RNA (Bryan strain grown in chick embryo fibroblast cultures) with various animal, plant, viral, bacteria and yeast DNA. Successful hybridization occurred in all cases excepting that of bacteria and yeast and the non-oncogenic denovirus types 2 and 4. DNA from adenovirus type 12 and SV40 showed significant homology. Further studies as to the nature of the hybridizing SV-RNA demonstrated a molecular size of about 5 by peak sucrose density gradient centrifugation. Paper chromatography and melting temperatures indicated that all the RSV-RNA hybrids were of similar base composition. It is believed that the cellular DNA hybridizing with RSV-RNA may be associated with the nuclear membrane.

70-456 STIMULATION OF DNA SYNTHESIS IN RESTING STAGE HUMAN FIBROBLASTS AFTER INFECTION WITH ROUS SARCOMA VIRUS. (E.) Macieira-Coelho, (Inst. Cancer Immunol., Villejuif, France), J. Hiu and E. Garcia-Giralt. Nature (London) 2(5199):1172, 1969.

Resting-stage cultures of WI-38 human embryonic fibroblasts exposed to Rous sarcoma virus (RSV), DNA synthesis was stimulated during the first 24 hours of exposure. A bacterial mucopolysaccharide and a synthetic polysaccharide also stimulated DNA synthesis. The DNA-stimulating effects of the bacterial polysaccharide and of RSV were abolished by hyaluronidase. Since successful infection requires cell division, it is suggested that stimulation of cell division by may be caused by some factor present in the preparations, but not identical with RSV, which affects viral replication.

70-457 ROUS SARCOMA IN BABOONS: DEVELOPMENT OF TUMOUR IN AN UNINOCULATED ANIMAL TREATED WITH CORTISONE. (E.) Kalter, S. S. (Southwest Found. Res. Ed., San Antonio, Tex.), A. K. Eugster, T. E. Vice, C. S. Kim and I. A. Ratner. Nature (London) 218(5144):884, 1968.

To enhance the oncogenic potential of Rous sarcoma virus (RSV; Schmidt-Ruppin strain), several RSV-inoc. baboons were treated with betamethasone-21-phosphate (B; 3 mg/kg/day). Non-infected controls were treated with B. One of the control animals, kept in the same rooms as the other animals which developed tumors following RSV inj., developed a typical RSV-type fibrosarcoma about 170 days after the first inj. of RSV into the animals (140 days after the appearance of the first tumor in the RSV-inj. baboons), at the approx. age of 7 mo., and died with multiple tumors 225 days after the beginning of the experiment. Complement fixation titers to RSV tumor antigen were below 1:10 at all times in this animal, except on 2 occasions at the time of onset of the tumor (at which time the titers were 1:20). RSV was not isolated from oral or rectal swabs of this animal. It is suggested that this baboon developed the tumor as a result of contact with RSV-inj. animals.

70-458 RECOVERY OF A HAMSTER-SPECIFIC, FOCUS-FORMING, AND SARCOMAGENIC VIRUS FROM A "NONINFECTIOUS" HAMSTER TUMOR INDUCED BY THE KIRSTEN MOUSE SARCOMA VIRUS. (E.) Klement, V. (Children's Hosp. Los Angeles, Calif.), J. W. Hartley, W. P. Rowe and R. J. Huebner. J. Nat. Cancer Inst. 43(4):925-934, 1969.

Tumor cells from *in vivo* passages 2 and 4 of a transplanted tumor, induced in DBA/2 mice by the Kirsten mouse sarcoma virus (Ki-MSV), induced mesenchymal sarcomas in 100% of newborn Syrian hamsters. Ki-MSV from a Fischer rat tumor (*in vivo* passage 3) also induced tumors in hamsters, but Ki-MSV from a virus-induced DBA/2 mouse tumor did not. A tumor line obtained from the mouse tumor cell-induced hamster sarcoma (Ki-MSV HT#2), was transplantable to adult hamsters; a tissue culture cell line (#59206), derived from transplant passage 5, was oncogenic to newborn hamsters. Preparations from both Ki-MSV HT#2 and the #59206 cell line were negative in complement fixation with mouse leukemia group-specific rat antisera. These cells were not infectious for Ki-MSV-sensitive mouse and rat cells. The tumor extracts contained a virus, designated Ki-MSV(O-H), which induced focus formation in hamster cells and was oncogenic in suckling hamsters. The Ki-MSV(O-H) virus was not neutralized by potent Ki-MSV antisera or by antisera to other viruses of the mouse leukemia-sarcoma complex (including the Moloney, Kirsten and Gross passage A leukemia viruses).

70-459 VIRAL INFECTION ACROSS SPECIES BARRIERS: REVERSIBLE ALTERATION OF MURINE SARCOMA

VIRUS FOR GROWTH IN CAT CELLS. (E.) Fischinger, P. J. (NCI, Bethesda, Md.) and T. E. O'Connor. Science 165(3894):714-716, 1969.

Infection of cat embryo fibroblast cultures with a centrifugally-induced aggregate of Moloney sarcoma virus (MSV) and feline leukemia virus (FLV), resulted in the formation of a defective focus-forming virus (designated FSV), which could be propagated in cat embryo cells but not in mouse cells. The FSV particles were apparently enveloped in the FLV virus coat. When FSV particles were aggregated with Moloney leukemia virus (MLV), the resulting virus could be propagated in Swiss mouse embryo cells, suggesting that the focus-forming genome of the sarcoma virus had again become enveloped with the MLV coat. Production of focus-forming MSV-FLV was readily reproducible by the centrifugation procedure. However, all attempts at trans-specific rescue of the defective MSV genome (from MSV-induced hamster tumors or cultures of these tumors, from infected cat cells, or by super-infection with FLV) failed.

70-460 PRODUCTIVE INFECTION AND MORPHOLOGIC ALTERATION OF HUMAN CELLS BY A MODIFIED SARCOMA VIRUS. (E.) Fischinger, P. J. (NCI, Bethesda, Md.) and T. E. O'Connor. J. Nat. Cancer Inst. 44(2):429-438, 1970.

In 4/4 human embryonic cell lines (derived from 2 normal and 2 cytogenetically abnormal embryos), Moloney sarcoma virus (MSV) apparently coated with feline leukemia virus (FeLV) envelope, alone or in association with FeLV, caused morphological transformation of the cells and was capable of replication. New defective MSV(FeLV) and FeLV (which could grow in both cat and human cells) were produced. MSV(FeLV) required active cell growth and showed selective tissue tropism. The human embryonic cell cultures could be chronically infected with either FeLV alone or with the MSV(FeLV) complex, but the Moloney leukemia virus pseudotype of MSV could not be propagated in these cells. A cell-free passage of MSV(FeLV) complex was established in human embryonic lung cells. FeLV alone was also capable of productively infecting some human cells, as shown by the induction of new helper virus for defective MSV(FeLV). It is suggested that MSV(FeLV) may be useful as an indicator for a possible human leukemia virus.

70-461 VIRUS-INDUCED SARCOMA OF MICE: INHIBITION BY A SYNTHETIC POLYRIBONUCLEOTIDE COMPLEX. (E.) Sarma, P. S. (NCI, Bethesda, Md.), G. Shiu, R. H. Neubauer, S. Baron and R. J. Huebner. Proc. Nat. Acad. Sci. USA 62(4):1046-1051, 1969.

Inj. of polyIpolyC in newborn NIH Swiss mice (100 µg s.c. on alternate days) two days prior to inoculation with Moloney (M-MSV (MLV))

and Friend (M-MSV(FLV)) pseudotypes of Moloney sarcoma virus, resulted in partial or complete suppression of tumors during the period of observation (20 days). When tumors did develop, they were small and localized in contrast to controls injected with phosphate-buffered saline. Inj. of polyIpolyC up to nine days after virus inoculation was also effective in preventing and reducing tumor size. A small number of tumors developed after treatment was stopped but when continued, this late development was prevented. In previously established tumors, polyIpolyC was found to suppress development and induce regression. Investigation revealed no direct action on sarcomas, and thus the action of PolyIpolyC was assumed to be the result of its induction of interferon.

70-462 FACTORS ANTAGONISTIC TO INTERFERON, EXTRACTED FROM TUMORS INDUCED BY MOUSE SARCOMA VIRUS IN THE HAMSTER. (Fr.) Chany, C. (CNRS Cancer Res. Inst., Villejuif, France), A. Grégoire and J. Lemaitre. C. R. Acad. Sci. [D] (Paris) 269(13):1236-1237, 1969.

Tumor cells of a strain (T-MSV) obtained by inoc. newborn hamsters with Moloney mouse sarcoma virus were inoc. i.m. into 3-weeks-old hamsters. Extracts derived from the resulting tumors were incubated with cells derived from Balb/c mouse embryos, prior to washing the preparations and incubating them with mouse hepatitis virus (MHV) for 3 multiplication cycles. As compared to controls, the multiplication of MHV was increased by 3-10 times, in 11/18 experiments. In a collateral study, L cells were treated with 20-40 or 200-400 U interferon, and then (after the interferon was removed) incubated with preparations of tumor extracts of hamster as above, prior to washing and infecting them with Indiana strain vesicular stomatitis virus. The extracts inhibited the antiviral effects of interferon significantly, at both interferon dose levels. Their activity was equal to 10-100 times the inhibitory activity of control extracts of muscle tissue cells, derived from the contralateral side of the tumor-bearing animals. The activity of the tumor extracts was not destroyed by trypsin or by heating to 56°C for 1 hour, nor was its production limited to any particular cell type.

70-463 ALTERATIONS IN THE CHARACTERISTICS OF SUGAR UPTAKE BY MOUSE CELLS TRANSFORMED BY MURINE SARCOMA VIRUSES. (E.) Hatanaka, M. (Flow Labs. Inc., Rockville, Md.), R. J. Huebner and R. V. Gilden. J. Nat. Cancer Inst. 43(5):1091-1096, 1969.

From the onset of morphological transformation, but not during the first 1-2 days after infection, mouse embryo tissue cultures infected with sarcoma viruses (Harvey sarcoma virus or the Gross or Rauscher pseudotypes) showed marked

increases in the uptake of D-glucose and D-mannose (the infected:uninfected uptake ratio was 20:1 by day 10 of infection) and a lesser increase in D-galactose uptake (the uptake ratio was 8:1 by day 10). This increased carbohydrate uptake was apparently dependent on the actual transformation process. The permeability of the cells to D-fructose, sucrose, uridine, thymidine, leucine and phosphate was not markedly affected, and the uptake of 3-O-methylglucose was reduced, in sarcoma virus-transformed cells. The Km values for glucose, mannose and galactose uptake in the sarcoma virus-transformed cells were about 10-fold lower than the values seen in uninfected mouse cells, SV40-transformed 3T3 cells, and cells transformed by the Rauscher, Friend or Moloney leukemia viruses. It is suggested that this alteration of membrane permeability to carbohydrates is specifically related to the presence of the sarcoma virus genome.

70-464 AN IMPROVED ADENOSINE TRIPHOSPHATASE ASSAY FOR PHYSICAL PARTICLES OF AVIAN MYELOBLASTOSIS VIRUS (AMV). (E.) Sekely, L. I. (New York Hosp., N. Y.) and A. M. Prince. Proc. Soc. Exp. Biol. Med. 132(3):1006-1012, 1969.

A modified adenosine triphosphatase (ATPase) assay for avian myeloblastosis virus (AMV; BA1 strain A) is described. When AMV was propagated *in vitro*, the relationship between ATPase activity and the virus conc. was linear, at AMV levels of 10^8 - 10^{12} particles/ml. When AMV was obtained from the plasmas of leukemic chickens, however, this ATPase assay was less sensitive; a linear reaction was observed down to levels of about 10^9 particles/ml, and lower levels could not be measured (perhaps because of the intrinsic buffering properties of plasma). The specificity of this reaction was confirmed by rate zonal and equilibrium density gradient centrifugation studies.

70-465 ON THE ROLE OF DNA SYNTHESIS IN AVIAN TUMOR VIRUS INFECTION. (E.) Duesberg, P. H. (U. California Virus Lab., Berkeley) and P. K. Vogt. Proc. Nat. Acad. Sci. USA 64(3): 939-946, 1969.

There is a need for early DNA synthesis by infecting avian tumor viruses (RAV-1, MAV-2, RAV-7 and RAV-50 of subgroups A, B, C and D, resp.; and RSV(0), even when the culture cells (chick embryo fibroblasts) have been preinfected with an avian tumor virus in the same taxonomic group. The DNA may be (1) a prerequisite for an unstable derepression of a cellular enzyme necessary in viral infection, not available for the later superinfection. (2) a cellular site for the virus. (3) genetically specific for the virus.

70-466 STUDY OF THE ANTIGEN SPECIFIC AGAINST THE GROUP OF ONCOGENIC AVIAN VIRUSES, IN CLONES OF HAMSTER CELLS TRANSFORMED BY ROUS VIRUS. (Fr.) Bataillon, G. (Inst. Radium, Orsay, France). C. R. Acad. Sci. [D] (Paris) 269(21):2156-2158, 1969.

The titer of an antigen (GS) specific against avian leukemia and sarcoma viruses was determined by the complement fixation technique in embryonal brown Leghorn fibroblasts (ELB) which had been transformed by the Bryan (B-) and Schmidt-Ruppin (SR-) strains of Rous sarcoma virus (RSV); in cells of a sarcoma induced in a newborn hamster by SR-RSV; in untreated ELB cells; in untreated BHK 21/13 cells (BHK); in cells of subclones derived from a clone (RB 12) of BHK which had been transformed by B-RSV; in cells of subclones derived from a clone (RS 2) of BHK which had been transformed by SR-RSV; and in cells of subclones obtained following a second transformation of RB 12 and RS 2 cells by polyoma virus. Over a period of several mo., representing a large number of cell generations, the GS titer was constant in subclones derived from RB 12 or RS 2. In both groups, high- and low-titer subclones were found, although all RS 2 subclones showed titers lower than those of the low-titer RB 12 subclones. The titers of both RB 12 and RS 2 subclones were lower than the titers of ELB cells which had undergone corresponding transformations. In all cases, the titers of subclones derived from cells undergoing a second transformation (by polyoma virus) were less than those derived from cells which had been transformed by RSV alone, possibly due to functional competition between the 2 genomes, with each finding only partial expression, or due to an inhibition of the expression of RSV genomes by the genomes of the polyoma virus.

70-467 FACTORS ANTAGONISTIC TO THE ANTIVIRAL ACTIVITY OF INTERFERON, EXTRACTED FROM VARIOUS HUMAN SARCOMAS. (Fr.) Chany, C. (Inst. Cancer Res., Villejuif, France), J. Lemaître and A. Grégoire. C. R. Acad. Sci. [D] (Paris) 269(25):2628-2630, 1969.

Evidence of *in vitro* tumor-stimulating or anti-interferon activity was investigated in extracts from 18 human angio-, myxo-, chondro-, fibro-, reticulo- or rhabdomyosarcomas, as compared to both untreated controls and controls which were pretreated with extracts of normal muscle tissue derived from each of the same donors. When embryonal Balb/c mouse cells were incubated with the extracts, prior to washing and infecting with mouse hepatitis virus, pretreatment with the tumor extracts resulted in an increase of 2-10 times the infectious virus titer on L cells in 15/15 instances, as compared to untreated controls. Cells which were pretreated with extract of normal muscle tissue were entirely

negative in 24/30 instances, positive in only 6/30. In a correlative study, L cells were treated with various conc. of interferon, then with tumor or muscle-tissue extract, prior to being infected with Indiana strain vesicular stomatitis virus. The sarcoma extracts inhibited the antiviral activity of interferon significantly; the muscle-tissue extracts showed somewhat less than 50% the same inhibitory activity. Both heating to 56°C for 1 hour and the addition of trypsin partially inactivated the inhibitory activity of the sarcoma extracts; and had no effect on the activity of the muscle-tissue extracts.

70-468 HUMAN LIPOSARCOMAS: TISSUE CULTURES CONTAINING FOCI OF TRANSFORMED CELLS WITH VIRAL PARTICLES. (E.) Morton, D. L. (NCI, Bethesda, Md.), W. T. Hall and R. A. Malmgren. Science 165(3895):813-816, 1969.

Cells obtained from the pleural effusion of a 60-yr.-old man with liposarcoma were used to obtain a tissue culture, which was passaged several times *in vitro* without morphological changes from the original liposarcomatous structure of the cells. Type C particles, morphologically similar to particles of the avian and mouse sarcoma viruses, were found in foci of transformed liposarcoma cells in tissue culture. These virus-like particles were seen only in foci of cells of a certain type, and were not seen in cells of a different morphological type found between the virus-containing foci in the same flask. Contamination of these cultures by avian or mammalian sarcoma viruses was ruled out. Serum from the pt. reacted with cytoplasmic antigens in the original liposarcoma and in the cultured liposarcoma cells. Results of several studies suggest the presence of a potentially defective viral genome in this tissue culture.

70-469 SUCCESSFUL TRANSPLANTATION OF LYMPHOSARCOMA IN CALVES TREATED WITH ANTI-LYMPHOCYTE SERUM. (E.) Donawick, W. J. (U. Pennsylvania Sch. Vet. Med., Kennett Square) C. Johnstone, J. G. Martens, D. C. Dodd, J. E. Martin and R. R. Marshak. J. Nat. Cancer Inst. 44(2):467-472, 1970.

Horse anti-bovine lymphocyte serum (ALS) was admin. to 2-week-old calves, beginning 13 days before transplantation (in and around the femoral lymph nodes) of single-cell suspensions of lymphosarcomas from 5 cows. ALS admin. was continued until death or signs of functional recovery of cellular immunity (demonstrated by skin allograft rejection). Lymphosarcomas developed in 10/14 calves in the primary tumor cell passage. The first and second serial passages (from 2 of the primary tumors in cows) yielded lymphosarcomas in 3/6 and 0/10 calves, resp. Histological examination and chromosomal analyses confirmed the success of the grafts.

Four calves developed generalized lymphosarcoma; in the other animals, the tumor spread from the inoc. site at least as far as the iliac lymph nodes. No particles resembling known leukemia viruses were seen in lymphomas or in normal tissues from these calves.

70-470 INCIDENCE OF LYMPHOCYTIC NUCLEAR PROJECTIONS IN BOVINE LYMPHOSARCOMA. (E.) Miller, J. M. (Dept. Vet. Sci., U. Wisconsin Madison), L. D. Miller, K. G. Gillette and C. Olson. J. Nat. Cancer Inst. 43(3):719-727, 1969.

Grade 2 or 3 lymphocytic nuclear projections (LNP) were found in tumors from 21/21 adult cattle with bovine lymphosarcoma, peripheral blood lymphocytes from 12/12 cows (of a multiple-case herd) with persistent lymphocytosis, 1/2 young animals with "adolescent thymic" lymphosarcoma, and peripheral lymphocytes from 3/7 cows (from the same multiple-case herd as the animals with lymphocytosis) with suspect lymphocytosis. No LNP were found in tumor tissues from 2 calves with generalized lymphosarcoma. In lymph node preparations from animals of a tumor-free herd, and in peripheral lymphocytes from hematologically normal animals of a multiple-case herd, LNP were infrequent and, when present, were classified as Grade 1 only. Relative frequencies of LNP were also high in tissues from 9/17 animals inoc. *in utero* with tumor tissue or blood from animals with lymphosarcoma.

70-471 ELECTRON MICROSCOPIC OBSERVATIONS ON A "C"-TYPE VIRUS IN CELL CULTURES DERIVED FROM A TUMOR-BEARING VIPER. (E.) Zeigel, R. F. (Roswell Park Mem. Inst., Buffalo, N. Y.) and H. F. Clark. J. Nat. Cancer Inst. 43(5):1097-1102, 1969.

Liver, heart, spleen, kidney, pancreas, salivary gland and tumor tissues were obtained from an Asian pit viper (*Vipera russelli*) with a spontaneous tumor (an edematous myxofibroma) of the connective tissue. The only tissue which could be serially passaged *in vitro* was the spleen. Cells from passages 48 or 52 of the spleen cell culture (the VSW cell line) contained a C-type budding virion, resembling the oncogenic RNA viruses of birds and mammals. The mature extracellular particles of this viper virus (which was antigenically distinct from certain known murine and avian C-type viruses) were structurally similar to virions of avian leukosis virus, although somewhat larger. No similar virus particles were found in the primary tissues (including the spleen and tumor) or in other culture lines.

70-472 NEOPLASTIC TRANSFORMATION AND DERIVATION OF A FOCUS-FORMING SARCOMA VIRUS IN CULTURES OF RAT EMBRYO CELLS INFECTED WITH A MURINE OSTEOSARCOMA (FBJ) VIRUS. (E.)

Rhim, J. S. (Microbiological Assoc., Inc., Bethesda, Md.), R. J. Huebner, W. T. Lane, H. C. Turner and L. Rabstein. Proc. Soc. Exp. Biol. Med. 132(3):1091-1098, 1969.

The FBJ mouse osteosarcoma virus induced neoplastic transformation in rat embryo cells *in vitro*. The transformed cells produced virus and complement-fixing (CF) antigen characteristic of the mouse leukemia-sarcoma virus complex. In newborn NIH Swiss mice, these transformed cells induced osteosarcomas, which were transmissible by cell-free extracts in newborn mice. Cell-free extracts of the mouse tumors also produced transformed foci *in vitro*. In newborn Fisher rats, inj. of the transformed rat embryo cells induced undifferentiated sarcomas, which also yielded virus and CF antigens.

70-473 TITRATIONS OF MAMMARY TUMOR VIRUS IN FRESH AND TREATED RIII MILK AND MILK FRACTIONS. (E.) Moore, D. H. (Inst. Med. Res., Camden, N. J.), N. Pillsbury and B. D. Pullinger. J. Nat. Cancer Inst. 43(6):1263-1273, 1969.

Freezing and thawing of undiluted skim milk from RIII/Haag mice (tumor incidence 79%) 1 time dropped the titer 2 logs (99% of bioactivity), and freezing and thawing 5 times dropped it 3 logs (99.9%). The loss of bioactivity was not as severe if the milk was diluted (saline) 100-fold before freezing. Little effect on the bioactivity was seen after exposing diluted or undiluted milk to 37°C for 18 hours. The bioactivity of fractions taken after centrifugation of milk concentrates on preformed gradients of ficoll and the content of B particles were unrelated. Tumor incidence was tested in BALB/c and C57BL/Haag mice. Incidence of the principal infection zone from the centrifuge tube increased from 10% at 10^{-1} dilution to 55% at 10^{-7} dilution. There was no relationship between tumor or nodule incidence and concentration of infectious particles, except where the dilution approached the endpoint.

70-474 MAMMARY-TUMOR VIRION STRUCTURES IN MOUSE MILK FRACTIONS. (E.) Sarkar, H. (Inst. Med. Res., Camden, N. J.), J. Charney and D. H. Moore. J. Nat. Cancer Inst. 43(6):1275-1288, 1969.

Milk pooled from RIII/Haag mice, virions were found in the cream, low-speed pellet and high-speed supernatant. Mammary tumor virus (MTV) B particles were found in the cream on study by electron microscopy (a new technique). They were of different sizes, but all nearly spherical. The cream extract and skim milk samples obtained after washing by the batch method gave strong positive tests for the MTV antigen. After centrifugation, an abundance of structures of cellular origin and B particles, many in aggregates or adhered to larger

structures, were found. The authors conclude that the unusual adhesive and cohesive properties of the B particle help explain the difficulty in isolating it in milk. A similar series of tests run on milk from C57BL/Haag mice gave negative results for B particles.

70-475 DEVELOPMENT OF AN INFECTIVITY ASSAY FOR MOUSE MAMMARY-TUMOR VIRUS. (E.) Charney, J. (Inst. Med. Res., Camden, N. J.), B. D. Pullinger and D. H. Moore. J. Nat. Cancer Inst. 43(6):1289-1296, 1969.

Mammary tumor virus (MTV)-containing milk from RIII mice was processed by density gradient centrifugation. When serial dilutions of the B3 density gradient zone (containing large numbers of MTV particles) were inoc. i.p. into C57BL mice, 54%, 85% and 86% of the first-, second- and third-lactation milks from these mice, resp., were positive for soluble MTV antigen (by the gel microdiffusion test). MTV antigen in the third-lactation milk predicted tumorigenesis; 85% of these antigen-positive mice developed mammary tumors after 18 mo. of observation. The presence of MTV antigen in the first-lactation milk could also predict tumorigenesis, since mice positive during the first lactation were always positive during the third lactation. It is suggested that antigen-positivity during the first lactation could be used to shorten the assay period. No tumors developed in antigen-negative mice. Definite 50% infective endpoints could be calculated by this method. The dose-response regression of this assay was characteristic of other virus dilution assays. In contrast to tumor development, this MTV infectivity assay time was short (3-3.5 mo.).

70-476 INFRASTRUCTURES, RELATIONS AND DISTRIBUTION OF VIRAL AND INFRAVIRAL PARTICLES IN INVASIVE OR METASTASIZING MAMMARY ADENOCARCINOMAS IN THE MOUSE. (Fr.) Thomas, J. A. (Ctr. Cell Physiol., Fac. Sci., Paris), E. Hollande, M. Henry and M.-C. Ducros. C. R. Acad. Sci. [D] (Paris) 269(2):265-268, 1969.

Electron microscopy of mouse mammary adenocarcinomas permitted definition of particles (A) which appeared to be precursors of the mature, free, mouse mammary tumor virus (B), and of several intermediate stages of development, linking the two. Maturation from one to the other form took place at the outer limits of the cell, inside Golgian vacuoles, or inside relatively large, multivesicular bodies. The development of envelopes (which were continuous with the cellular membrane, plasmalemma, or other membrane-containing structure, and which contained many spicules) was characteristic of the first step in maturation, finally resulting in dehiscence and setting the mature B particle free. In the fully matured B particle, an hexagonal, excentric nucleoid appeared as a

filamentous structure, attached to the dense, internal face of the viral envelope and rolled up upon itself to form a nucleocapsid. Following the eventual rupture of the viral envelope, this exposed nucleocapsid formed the only enduring residuum of the particle. Also demonstrated in these studies were numerous infraviral particles, occasional tubules (presumably of viral origin) in the vicinity of groups of A particles, and type C leukemic viruses which appeared to be present in a more or less consistent, quantitative relationship to the number of mammary tumor viruses in the same area (all forms).

70-477 THE CYCLE OF THE MOUSE MAMMARY ADENOCARCINOMA VIRUS AND ITS RELATIONSHIP WITH LACTIC SECRETION. (Fr.) Thomas, J. A. (Ctr. Cell Physiol., Paris), E. Hollande, M. Henry and M.-C. Ducros. C. R. Acad. Sci. [D] (Paris) 269(3):396-399, 1969.

In the maturation cycle of mouse mammary adenocarcinoma, precursor particles (A) develop into mature viral particles (B), whose eventual rupture exposes the enclosed nucleocapsid in the form of an infraviral particle (IV) which appears to be the active infectious agent. The remainder of B (Br) is completely separated from IV. Although such maturation takes place most often just inside the plasmalemma, it can also take place inside the Golgi apparatus, with or without the simultaneous formation of lactic secretion, or inside the relatively large, multivesicular bodies, from which viral particles may be liberated into the hyaloplasm, initiating a process of autoinfection. Large numbers of IV and Br particles are found in the secreted milk, coming from all of these sources. (Those coming from the Golgi apparatus pass directly into and through the lactophoric canaliculi.) The virus-containing milk sometimes forms relatively large clots, containing pockets which are completely filled with virus particles. In any case, the amount of virus which the newborn animal receives in the course of nursing is considerable.

70-478 HIGH-YIELD ISOLATION OF MOUSE MAMMARY TUMOR VIRUS. (E.) Bond, H. E. (NCI, Bethesda, Md.) and W. T. Hall. J. Nat. Cancer Inst. 43(5):1073-1082, 1969.

A method of high-yield isolation of mammary tumor virus (MTV) in a high state of purity is described, employing rate-zonal centrifugation followed by isopycnic banding in a Ficoll in heavy-water gradient. Frozen and thawed samples of MTV, obtained in this way from C3H mouse milk, induced mammary tumors at a 10^{-4} dilution.

70-479 PRODUCTION OF VIRUS-CONTAINING STRAINS OF MAMMARY ADENOCARCINOMA CAPABLE OF INDUCING GENERALIZED CANCERIZATION IN THE MOUSE.

(Fr.) Thomas, J. A. (Cell. Physiol. Ctr., Biol. Lab., Paris). C. R. Acad. Sci. [D] Paris 269(1): 117-120, 1969.

Eight female white mice of a strain which was not genetically pure, belonging to 3 different, experimental groups developed mammary adenocarcinomas following inj. of DNA derived from ascitic carcinoma Krebs 2. In the group which was most affected, 6/10 developed the tumors, while 1/10 developed an anaplastic carcinoma of the liver and spleen. Passage by grafting was extremely difficult in adults; however it was relatively successful in both male and female, newborn mice of the same strain and in newborn Swiss and CD₁ mice. In all 3 strains, occasional successes were also obtained in immature mice (C₃He/B, AKR, C₅₇Br/cd, R III/Ko and Balb/c mice were resistant to grafting, however). The most receptive sites were the s.c. tissues of the back, back of the neck, and head. Craniodorsal tumors infiltrated nearby muscular and osseous tissues rapidly, sometimes destroying a section of the vertebral column or extending to the thymus, glands and ganglia of the neck, thoracic and abdominal cavities, and/or cranium. The most frequent sites of metastasis were the kidneys, lungs, spleen, omentum, liver, female genital organs and external male genitalia. Cerebral metastases were also seen fairly frequently. Tumor takes were not enhanced by cortisone, 6-mercaptopurine, methotrexate, Krebs 2 DNA, asparagine or (attempted only in females) depot estradiol or depot progesterone.

70-480 ORGANIZATION AND DIFFERENTIATION OF THE MATURE PARTICLE OF MOUSE MAMMARY TUMOR VIRUS. (Fr.) Thomas, J. A. (Ctr. Cell Physiol. Biol. Lab., Paris), E. Hollande, M. Henry and M.-C. Ducros. C. R. Acad. Sci. [D] (Paris) 269(24):2471-2474, 1969.

Electron photomicrographic studies of T III mouse mammary tumor virus particles confirmed the occasional existence of a caudal prolongation of the envelope which was visible both by negative contrast and in ultrafine sections. This flexuous, thornlike "tail" was 315-500 mμ long and 30-40 mμ wide, with a terminal part which appeared to expand into a sort of ampule measuring 40-50 mμ in diameter. In some cases, it appeared to be firmly attached to the envelope of the particle; in some, the envelope was visibly dehiscent at this point. In others, the "tail" had fragmented into a series of oval vesicles; in still others, 2 or more caudal prolongations had anastomosed, joining together to form thin filaments as much as 800 mμ long, sometimes separated entirely from the viral particles involved, sometimes still joined to them. Such filaments were clearly distinguishable from the cytoplasmic tubules containing A particles, which were seen occasionally. The presence of a caudal prolongation, filament, or fractionated vesicles was invariably accompanied

by lysis of both enveloped nucleocapsids and the mature B particles which such processes frequently appeared to envelop.

- 70-481 HEREDITARY INFECTIONS WITH MAMMARY TUMOR VIRUSES IN MICE. (E.) Bentvelzen, P. (Radiobiol. Inst. TNO, Rijswijk, Netherlands) and J. H. Daams. J. Nat. Cancer Inst. 43(5): 1025-1035, 1969.

Male transmission, egg-borne transmission and extreme susceptibility to the plaque-inducing strain of mammary tumor virus (MTV-P) are controlled by the gene Ms^E in strain GR mice. This gene does not cause susceptibility to the standard strain (MTV-S; the "milk agent"), but the alleles of Ms^E control the susceptibility to both MTV-S and the less virulent MTV-P. In C3Hf mice, genes influence male transmission of only the low-oncogenic strain (MTV-L), without producing an extreme susceptibility to MTV-L. It is suggested that hereditary infections of this type result from virus transmission as a genetic factor of the host. Virus release is repressed in some strains (such as C57BL), but the virus is released by germinal mutations in the controlling genes of mice of other strains (such as GR and C3Hf). The repressor preventing the release of genetically-transferred virus may also induce resistance to superinfection with MTV-P or MTV-S, by interfering with the replication of these viruses.

- 70-482 ANTIGENIC AND ONCOGENIC PROPERTIES OF A CELL LINE DERIVED FROM A HAMSTER BRAIN TUMOR INDUCED BY SIMIAN ADENOVIRUS 7. (E.) Pauluzzi, S. (Baylor U. Coll. Med., Houston, Tex.) and F. Rapp. J. Nat. Cancer Inst. 43(5): 165-1173, 1969.

Cells from a hamster brain tumor (HBT), induced in newborn Syrian hamsters by intracerebral (i.c.) inj. of simian adenovirus 7 (SA7), were adapted to in vitro growth after 1-3 passages on irradiated feeder layers of newborn hamster brain cells. The HBT cells contained virus-specific tumor (T) antigen(s) in the cytoplasm, but not in the nuclei. Sera from HBT-bearing hamsters reacted with SA7-infected green monkey or human embryonic kidney cells, but not with purified SA7. The sera contained no SA7-neutralizing antibodies. Some cross-reactivity with T antigens of several human adenovirus serotypes was found. It is suggested that the HBT cells contain a virus-specific, nonstructural SA7 antigen, perhaps an adenovirus group-specific antigen. All attempts to rescue infectious SA7 from the HBT cells were unsuccessful. In weanling hamsters, HBT cells produced astrocytoma-type tumors after i.c. inj. The HBT cells, as well as cells from a tumor induced by s.c. inj. of SA7, were more oncogenic to weanling hamsters after i.c. inj. than after s.c. inj. Immunization with SA7 partially protected the

animals against i.c. or s.c. challenges with HBT cells. It is suggested that SA7 can induce an antigen leading to rejection, and that SA7-transformed brain cells contain a transplant rejection antigen.

- 70-483 ESTABLISHMENT OF A MALIGNANT CELL LINE DERIVED FROM HUMAN ADENOVIRUS TYPE 12-INDUCED HAMSTER TUMOR IN TISSUE CULTURE. (E.) Makino, S. (Kitasato Inst., Japan), N. Maehara, K. Sasaki, M. Nakagawa, M. Takada, S. Kasahara and A. Kawamura, Jr. Kitasato Arch. Exp. Med. 41(3-4):49-57, 1968.

A tumor induced in a golden hamster by human adenovirus type 12 was successfully established in continuous cell culture. The tumorigenicity of the cultured cells at passage 61 was demonstrated by s.c. inj. of the cells into 4-wk.-old golden hamsters, which developed tumors histologically similar to those induced by inoc. of human adenovirus type 12. No infectious virus was detected in the cultured tumor cells. Complement fixation tests revealed in the cultured tumor cells T antigens associated with infection by adenovirus type 12. Some sera from hamsters bearing adenovirus type 12-induced tumors or tumors transplanted from cultured tumor cells reacted with adenovirus type 12 antigen. Fluorescent antibody staining using antiserum from hamsters bearing adenovirus type 12-induced tumors showed nuclear and cytoplasmic specks in cultured tumor cells.

- 70-484 TRANSFORMATION OF RODENT CELLS BY ADENOVIRUS 19 AND OTHER GROUP D ADENOVIRUSES. (E.) McAllister, R. M. (U. Southern California Sch. Med., Los Angeles), M. O. Nicolson, G. Reed, J. Kern, R. V. Gliden and R. J. Huebner. J. Nat. Cancer Inst. 43(4): 917-923, 1969.

The properties of the oncogenic subgroup D of human adenoviruses (AV's), consisting of the 14 AV's belonging to hemagglutination group 2 and AV types 20, 25 and 28, are discussed. AV types 9, 10, 13, 15, 17, 19 and 26 from this new subgroup induced transformation in NIL-2 hamster cells and in primary cultures of Fischer rat embryonic cells. NIL-2 cells transformed by AV types 19 and 26 also induced typical AV tumors in hamsters. Cells from these tumors, like cells transformed by other viruses of this subgroup, shared a common tumor (T) antigen but contained no virus-specific messenger RNA.

- 70-485 TRANSFORMATION OF RODENT CELLS BY SIMIAN ADENOVIRUS SA-7. (E.) McAllister, R. M. (U. Southern California Sch. Med., Los Angeles), J. L. Riggs, G. Reed and I. Macpherson. Proc. Soc. Exp. Biol. Med. 131(4): 1442-1445, 1969.

NIL-2 hamster cells and primary cultures of Fischer or Hooded Wistar rat embryo cells were transformed by exposure to simian adenovirus 7 (SA7; C8 strain). The transformed foci resembled those induced by adenovirus (AV) types 1, 2, 3 and 12. Cell lines were derived from SA7-transformed rat and NIL-2 cells. SA7-transformed NIL-2 cells induced typical adenovirus tumors (undifferentiated sarcomas) at the inj. site in newborn or adolescent hamsters. Transformed NIL-2 cells contained the tumor antigen of SA7, but not those of AV types 7 or 12, SV20 or SV40. SA7 transformed NIL-2 cells more efficiently than AV types 7 or 12; in rat cells, the efficiencies of SA7 and of AV types 1 and 12 were about the same.

70-486 ISOLATION OF HISTONES FROM VIRUS-INDUCED TUMORS. (E.) Boulanger, P. A. (INSERM Res. Unit. Protein Biochem., Lille, France), F. Jaume, Y. Moschetto and G. Biserte. FEBS Letters 4(4):291-294, 1969.

Nucleohistones from hamster tumors induced by adenovirus-12 or adenovirus-2/SV40 and from adenovirus 2-transformed rat embryonic cells, were fractionated by gel electrophoresis. All tumors studied contained histones of essentially the same composition. The slowest-migrating band (Fraction 1) was lysine-alanine-rich; the faster-moving band (F2(a)1) was glycine- and arginine-rich, and the intermediate bands (F2(a)2, F2b and F3) were rich in arginine and lysine. Histones from calf thymus and other animal tissues differed from these tumor cells in some ways, notably a higher content of acidic amino acid. This difference was especially marked in the F1 fractions, which showed a higher acidic amino acid content and lower lysine and alanine contents in the normal cells, compared to the tumor cells.

70-487 ADENOVIRUS-12 TRANSFORMATION OF GERBIL LUNG CELLS. (E.) Shaw, G. J. (Dalhousie U., Halifax, Nova Scotia) and E. S. McFarlane. Canad. J. Microbiol. 15(6):583-586, 1969.

Adenovirus-12 transformed gerbil lung cells in vitro. No infectious virus could be recovered from the transformed cells or visualized by electron microscopy. The transformed cells contained T antigen by the complement fixation test prevented the development of tumors in hamsters previously inoc. with adenovirus-12, and exhibited elevated tRNA methylase activity.

70-488 INDUCTION OF TRANSMISSIBLE LYMPHOMAS IN SYRIAN HAMSTERS BY APPLICATION OF DNA FROM VIRAL HAMSTER PAPAPOVIRUS-INDUCED TUMORS AND BY CELL-FREE FILTRATES FROM HUMAN TUMORS. (E.) Graffi, A. (German Acad. Sci., Berlin), E. Bender, T. Schramm, W. Kuhn and F. Schneiders.

Proc. Nat. Acad. Sci. USA 64(4):1172-1175, 1969.

DNA from skin epitheliomas containing papovavirus induced lymphomas in 40 - 50% of newborn hamsters (this effect was eliminated by DNase and not RNase), while cell-free extracts from human tumors (including stomach, pancreas, lung, ovary and mammary) had varying effectiveness in inducing lymphomas. DNA from the induced lymphomas and from transplanted epitheliomas contained no papova viral particles and did not induce lymphomas. Cell-free extracts of normal human tissue had no leukemogenic effects. Apparently the hamster papova virus or its DNA induces lymphomas and human tumor extracts may activate a latent hamster leukemia virus. In all cases, induction or passage of lymphomas depended on using a colony of hamsters free of spontaneous lymphomas and skin epitheliomas.

70-489 SPECIFIC SURFACE ANTIGEN IN SHOPE PAPILLOMA CELLS. (E.) Ishimoto, A. (Aichi Cancer Ctr. Res. Inst., Nagoya, Japan) and Y. Ito. Virology 39(3):595-597, 1969.

In up to 5% of cells cultured from rabbit papillomas induced by Shope papilloma virus, an annular or semicircular pattern of immunofluorescence was observed at the cell membrane, using antiserum from tumor-bearing rabbits. This pattern was not observed with antiserum against Shope papilloma virus.

70-490 CANINE PAPILLOMA: THE STRUCTURAL CHARACTERIZATION OF ORAL PAPILLOMA VIRUS. (E.) Watrach, A. M. (U. Illinois Coll. Vet. Med., Urbana), L. E. Hanson and R. C. Meyer. J. Nat. Cancer Inst. 43(2):453-458, 1969.

Canine oral papilloma (COP) virus isolated from a 1.5-yr.-old beagle with multiple papillomatous growths in the oral cavity and anterior part of the pharynx, and observed in sections of the neoplastic tissue, tended to accumulate in large numbers in the nuclei of affected cells; and had a propensity to aggregate in crystalline formations, in the form of either rafts possessing a plane lattice or space-oriented aggregates with a recognizable space lattice. Some particles were seen in loosely dispersed groups throughout the nucleoplasm. Individual virus particles ranged from 470-530A (av. 490A). In negatively stained preparations virus particles av. 560 A. The outer shell was formed from a close-packed array of morphological units regularly disposed over the surface. Analysis of the configuration of the morphological units indicated that the shell of COP virus consisted of 72 morphological units and had a skew surface lattice in common with viruses of the papilloma-polyoma group.

70-491 MALIGNANT TRANSFORMATION OF HAMSTER CELLS BY CELL-FREE EXTRACTS OF BOVINE PAPILLOMAS (IN VITRO). (E.) Geraldes, A. (Gulbenkian Inst. Sci., Oeiras, Portugal). Nature (London) 222(5200):1283-1284, 1969.

Bovine papilloma virus (BPV), obtained from 3 different bovine papillomas, induced morphological transformation, after 4-8 days of exposure, in second-passage cultures of embryonic cells derived from non-inbred Syrian hamsters. Extracts from normal bovine skin did not induce transformation. Unexposed control cultures did not undergo transformation. No BPV particles were observed in the transformed cells. As the number of *in vitro* subcultures of the transformed cells increased, the capacities of these cells to produce tumors at the site of s.c. inj. in 24-day-old syngeneic hosts also increased. Control cultures never induced tumors, even after more than 1 yr. of observation.

70-492 T-ANTIGEN AND DNA SYNTHESIS IN MACROPHAGES INFECTED WITH POLYOMA VIRUS. (E.) Mallucci, L. (Roy. Postgrad. Med. Sch., London). Nature (London) 223(5206):630-632, 1969.

Cultures of peritoneal macrophages from C57BL and NIH albino mice showed a marked stimulation of cellular DNA synthesis, not followed by mitosis, resulting from abortive infection with polyoma virus (S.E. wild type). Production of T antigen was detected (36 hours after infection) only in the C57BL cells. It is suggested that activation of host cell DNA synthesis is not correlated with T antigen production.

70-493 BIOCHEMICAL EVIDENCE FOR INDUCTION BY POLYOMA VIRUS OF REPLICATION OF THE CHROMOSOMES OF MOUSE KIDNEY CELLS. (E.) Hancock, R. (Swiss Inst. Exp. Cancer Res., Lausanne, Switzerland) and R. Weil. Proc. Nat. Acad. Sci. USA 63(4):1144-1150, 1969.

Viral-induced (wild type Py virus) synthesis of chromosomal proteins accompanied the observed increase in DNA replication, as determined by the assay of the incorporation of lysine-¹⁴C into these proteins. It was shown: (1) up to 15 hr. lysine-¹⁴C was incorporated into chromosomal protein at the same rate in both Py-infected and mock-infected cultures. (2) from 15-30 hr. synthesis in the Py-infected culture increased until it contained 50-60% more chromatin. Chemical determinations show the same mass ratios of histones and non-histone protein as in eukaryotic cells. (3) Addition of 5-fluorodeoxyuridine (FUDR) inhibited incorporation of lysine-¹⁴C. Reversal of this inhibition with deoxythymidine, a specific blocker of FUDR, indicated that Y-induced DNA synthesis is a prerequisite for stimulation of histone synthesis. (4) Non-histone chromosomal protein was found to incorporate

lysine-¹⁴C at a comparable rate to the increased uptake by histones.

70-494 THE REPLICATION OF THE RING-SHAPED DNA OF POLYOMA VIRUS, I. IDENTIFICATION OF THE REPLICATIVE INTERMEDIATE. (E.) Bourgaux, P. (Salk Inst. Biol. Stud., San Diego, Calif.), D. Bourgaux-Ramoisy and R. Dulbecco. Proc. Nat. Acad. Sci. USA 64(2):701-708, 1969.

Whole mouse embryo cultures, infected with polyoma virus (2×10^8 plaque-forming units in 0.4 ml) were labeled with H³-thymidine (25 μ C/ml), after which the DNA was extracted and band centrifugation was performed. The labeled viral DNA molecules were found in three main forms: component I (high molecular wt. in a superhelical configuration); component II,* believed to be the replicative intermediate (the molecules contain the most label after a short exposure, but their label moves towards component I molecules as length of labeling increases) component II (low molecular weight). Characteristics of component II* molecules are: (1) they are ring shaped and nicked; (2) they are larger than the component II* molecules; and (3) they contain strands of various lengths, the largest of which corresponds to that of mature viral DNA (<16S after 10 minute labeling; 18S peak visible after 30 min.).

70-495 A STUDY ON THE TRANSCRIPTION OF THE POLYOMA VIRAL GENOME. (E.) Hudson, J. (Swiss Inst. Exp. Cancer Res., Lausanne, Switzerland), D. Goldstein and R. Weil. Proc. Nat. Acad. Sci. USA 65(1):226-233, 1970.

In primary mouse kidney cultures infected with wild-type polyoma virus (PV), synthesis of PV-induced viral and cellular DNA began at 12-13 hr. and reached max. levels (60-80% of the cells) in about 30 hr. Uridine-³H-labeled PV-RNA was barely detectable before 12 hr. and reached a max. level (3-6% of total radioactivity) in about 30 hr. Virus-specific RNA transcribed in the absence of detectable viral DNA was termed "early" PV-RNA; virus-specific RNA transcribed after DNA synthesis was termed "late" PV-RNA. Addition of 5-fluoro-2'-deoxyuridine (FUDR) to the medium 2 hr. after infection permitted a small amount (5% of normal) of viral RNA to appear in 30-36 hr.; when the effects of FUDR were reversed by deoxythymidine, PV-DNA and -RNA increased to levels found in normal parallel cultures (about 7 hr.). It is suggested that the rate of late RNA transcription depends on the amount of PV-DNA, and that early RNA comprises a small amount of the total and may be synthesized late in the infection. Hybridization studies showed that the bulk of the late RNA corresponds to the polycistronic transcript of most of the genetic information of PV-DNA. Early PV-RNA may be transcribed from integrated viral DNA.

70-496 DIFFERENTIAL ULTRAVIOLET RADIATION SENSITIVITY OF CERTAIN FUNCTIONS OF THE POLYOMA VIRUS. (Fr.) Meyer, G. (Reg. Ctr. Cancer, Marseille, France), A. M. Lhérisson-Straboni and H. Bonneau. *Int. J. Cancer* 4(4): 520-532, 1969.

The UV sensitivities of 2 target areas of the polyoma virus (PV) were studied in PV-infected BHK-21 hamster fibroblasts and in hamsters inoc. with 2 PV-induced transplantable tumors (CT-54 and its derivative H-333). The results indicated that about 50% of the viral genome is required to induce nuclear T antigen, whereas about 16.6% of the genome is required to induce the homograft rejection antigen. It is concluded that the more sensitive attribute of PV (the portion determining nuclear T antigen) is present in cells transformed by the more UV-resistant portion of the viral genome. This was explained by the postirradiation ability of a larger number of virions to cause abortive infection of cells which can induce transformation, which results in a relative increase in transforming ability.

70-497 KINETICS OF MULTINUCLEATED CELLS IN TUMOR CULTURES OF THE HAMSTER POLYOMA SYSTEM. (Fr.) Berebbi, M. and H. Bonneau (Sci. Res. Group Human Tumors, Marseille, France). *C. R. Soc. Biol. (Paris)* 163(2):481-484, 1969.

Small-plaque polyoma virus inoc. into hamsters of a heterozygotic line induced transplantable tumors of the CT 54 type. Following passage in the animal, these tumors were maintained in vitro through 20 passages and comparative morphologic and cytogenetic studies were made on cells from each passage which were exposed to colchicine (0.5 µg/ml culture for 12 hours), as well as cells which were not so exposed. In both cases, a significant number of multinucleated cells were found in the first and second in vitro passages, with the greatest incidence occurring in the second passage and the incidence decreasing progressively thereafter until it became extremely slight from the thirteenth passage on. Immunologic tests confirmed that the polyoma marker also disappeared progressively, in parallel fashion, until the cells became negative by the thirteenth passage, at which time tumorigenic activity was no longer in evidence. The phenomena suggested that the multinucleated cells resulted from the presence of a part of the viral genome, integrated with the cellular genome.

70-498 APPEARANCE AND PERSISTENCE OF A SPECIFIC INHIBITOR IN SYRIAN V HAMSTER CELLS INFECTED WITH POLYOMA VIRUS. (Fr.) Cramer, R. (Inst. Radium. Biol., Orsay, France). *C. R. Acad. Sci. [D] Paris* 268(25):3142-3145, 1969.

Following infection with small-plaque polyoma virus, BKH 21 Syrian hamster cells contained a

specific inhibitor which prevented replication of the virus in embryonic mouse cells but did not inhibit replication of Indiana strain vesicular stomatitis virus. The inhibitor was demonstrable from the twelfth hour post-infection; attained max. activity at the sixteenth hour, at which time the stimulation of thymidine incorporation into the infected cells began to decline. The inhibitor had no effect on the replication of vaccinia virus in BHK 21 cells. The presence of the inhibitor was demonstrable in clones of BHK 21 cells transformed by polyoma virus and in a clone of BHK 21 cells which had undergone double transformation by polyoma virus + Rous sarcoma virus, but not in a clone transformed by Rous sarcoma virus alone or in cells undergoing "spontaneous" transformation. Although it was also demonstrable in rat cells infected with polyoma virus, it could not be demonstrated in mouse cells or in hybrid mouse-hamster cells infected in the same way.

70-499 CONTROL OF THE REVERSION OF PROPERTIES IN TRANSFORMED CELLS. (E.) Rabinowitz, Z. (Weizmann Inst. Sci., Rehovot, Israel) and L. Sachs. *Nature (London)* 225(5228):136-139, 1970.

When hamster embryo cells were transformed by polyoma virus and seeded for cloning at various densities, the frequency of variant cells possessing certain reverted characteristics was highest at low density (3×10^2 cells/5-cm Petri dish). The variants re-reverted to transformed cells during subsequent cell crowding; the reversion could be prevented by inhibiting cell multiplication. The variant cells contained a higher number of chromosomes than did the transformed cells.

70-500 REPRODUCTIVE CAPACITY AND VIABILITY AT HIGHER TEMPERATURES OF VARIOUS TRANSFORMED HAMSTER CELL LINES. (E.) Kachani, Z. F. C. (U. Cincinnati Coll. Med., Ohio) and A. B. Sabin. *J. Nat. Cancer Inst.* 43(2):469-480, 1969.

Syrian hamster embryo cultures transformed in vitro by X-irradiation or by dimethylnitrosamine, reproduced at 41-41.3°C. Cells transformed in vitro by polyoma virus or simian virus 40 (SV40) reproduced at 41.6°C. However, cells transformed in vivo by these viruses did not have reproductive ability at higher temperatures. Cell cultures from serially transplanted SV40 and polyoma virus tumors produced in vivo had lower viability at 41.3-41.6°C than those derived from a serially transplanted, sodium cholate tumor produced in vivo, or cultures transformed in vitro by these viruses, dimethylnitrosamine, X-irradiation or untreated hamster embryo cultures. Temperatures that inhibited multiplication did not kill the cells. Results indicated that reproductive capacity (rct) and viability (t) are determined by different factors (genes) at higher temperatures: Cloned or

uncloned rct/41.6°C⁺, t/41.6°C⁺ culture of cells transformed *in vitro* by SV40 or polyoma virus, transplanted in weanling hamsters, produced tumors that yielded rct/41.6°C⁻, t/41.6°C⁻ cultures.

70-501 SV40 GENE ACTIVITY DURING LYTIC INFECTION AND IN A SERIES OF SV40 TRANSFORMED MOUSE CELLS. (E.) Martin, M. A. (NIH, Bethesda, Md.) and D. Axelrod. Proc. Nat. Acad. Sci. USA 64(4):1203-1210, 1969.

During lytic infection (African Green monkey kidney cells), 50% of SV40 DNA (equivalent to one DNA strand) was saturated with an excess of lytic RNA. RNA from mouse transformed cell lines which yielded virus following cell fusion (SV-T2;SV-PY-11; SV-935C) saturated 30-50% of SV40 DNA, while RNA from lines not yielding virus (SV-UV-155;SV-UV-30-1), saturated only 15-20%. Saturation-competition reactions between the lytic and transformed cell RNA indicated the same sites on the SV40 DNA were being occupied. Proposed mechanisms for the different expression of viral DNA are: (1) minor differences, relative amounts or sequential appearance of virus-specific RNA, (2) inability to separate viral genome in transformed cell host, (3) a block in translation.

70-502 RUTHENIUM RED-STAINED COAT OF NORMAL AND SIMIAN VIRUS 40-TRANSFORMED CELLS. (E.) Vorbrott, A. (Wistar Inst. Anat. Biol., Philadelphia, Pa.) and H. Koprowski. J. Nat. Cancer Inst. 43(6):1241-1248, 1969.

Electron microscopic studies were performed on the ruthenium red-stained coat (RRSC) on the surface of normal, neoplastic (nonviral) and simian virus 40(SV40)-transformed cell lines of human, monkey and hamster origin. The thickness of the RRSC of normal cells was variable and in many cells, relatively thick. No characteristic changes in the thickness were seen in virus-transformed cells. Extensive undulation of the free surface of the superficial layer of cells, with many protrusions and microvilli covered by a thick layer of RRSC were seen in SV40 transformed cells. The nonviral neoplastic cells showed some undulation, but the RRSC was thinner. Normal cell surfaces were mainly smooth.

70-503 A NONDEFECTIVE (COMPETENT) ADENOVIRUS-SV40 HYBRID ISOLATED FROM THE AD.2-SV40 HYBRID POPULATION. (E.) Lewis, A. M., Jr. (Nat. Inst. Allergy Infect. Dis., Bethesda, Md.), M. J. Levin, W. H. Wiese, C. S. Crumpacker and P. H. Henry. Proc. Nat. Acad. Sci. USA 63(4):1128-1135, 1969.

An example of genetic heterogeneity within and between hybrid populations, this adenovirus type 2 (Ad.2)-SV40 hybrid (designated AD.2*ND₁) was

unique in being non-defective, in replicating with 1-hit kinetics in human embryo kidney and African green monkey kidney (AGMK) cells, and in inducing an SV40-specific antigen differing from the SV40 viral and T antigens. Particles inducing this antigen were neutralized only by an Ad.2 antiserum. The antigen reacted by immunofluorescence and complement fixation only with sera from hamsters with SV40-induced tumors. A morphologically similar antigen was isolated from infected cells of 3 species. Cells infected with AD.2*ND₁ contained SV40-specific DNA. Since the hybrid did not induce T antigen, but replicated in AGMK cells, the presence of separate loci for the T antigen and for adenovirus enhancement in AGMK cells is suggested. No evidence of pathogenicity or transforming ability was found.

70-504 "RESCUED" SV40: INCREASED TRANSFORMING EFFICIENCY IN MOUSE AND HUMAN CELLS. (E.) Todaro, G. J. (NCI, Bethesda, Md.) and K. K. Takemoto. Proc. Nat. Acad. Sci. USA 62(4):1031-1037, 1969.

After recovery from transformed mouse (3T3 and Balb/3T3) and human tissue cells (L.S. and B.L.) the small plaque size mutant of SV40 showed the greatest increase in transforming ability, the minute plaque size less and the large plaque size little or none. Neither the minute nor the small plaque viruses could act as a helper for the large. The recovered virus in each case demonstrated the same host range, plaque type, temperature sensitivity and ability to induce cellular DNA synthesis as the parental virus. The production of SV40 T antigen paralleled the transforming ability in both the parental and the recovered viruses. In one viral strain (SV-S-68) increased transforming ability was undiminished even after two passages through monkey kidney. The mechanism of change in transforming properties was attributed to either a selection process or a host-induced modification.

70-505 SURFACE-SPECIFIC CHARACTERISTICS OF A CONTACT-INHIBITED CELL LINE CONTAINING THE SV40 VIRAL GENOME. (E.) Pollack, R. E. (New York U. Med. Ctr., N. Y.) and M. M. Burger. Proc. Nat. Acad. Sci. USA 62(4):1074-1076, 1969.

Five rat and mouse fibroblast cell lines were analyzed for agglutinability by wheat germ agglutinin (3-1000 µg/ml). Agglutination was directly correlated with saturation density, an indication of the availability of specific receptor sites for the agglutinin. One SV40-transformed cell line (SV101), with poor contact inhibition, showed the greatest agglutinability. When the receptor sites on non-agglutinating cells were exposed by digestion with a protease, the cells became as agglutinable as SV101. The mechanism relating the exposed surface receptor to the transformed state is unknown.

- 70-506 MORPHOLOGICAL AND BIOCHEMICAL STUDIES OF VIRUS (SV40) TRANSFORMED PROSTATIC TISSUE. (E.) Fraley, E. E. (NCI, Bethesda, Md.) and D. F. Paulson. J. Urol. 101(5):735-740, 1969.

Prostatic tissue from golden hamsters, divided into lobes, was cultured in vitro, transformed by infection with simian vacuolating virus 40, and inj. s.c. into irradiated, adult, male hamsters, which readily developed transplantable tumors. The size of tumors 14 days after isologous transplantation was markedly reduced in 12 orchiectomized hamsters receiving 12 mg stilbestrol at the time of transplantation followed by 3 weekly inj. of 4 µg estradiol, in 12 hamsters receiving 50 µg testosterone daily, and in 12 orchiectomized hamsters receiving both testosterone and the estrogens, as compared to untreated hamsters. These hormonal treatments also eliminated or reduced the rise in serum alkaline phosphatase which followed transplantation in controls.

- 70-507 PROPAGATION AND BEHAVIOR IN CHICKEN KIDNEY CULTURES OF THE AGENT ASSOCIATED WITH CLASSICAL MAREK'S DISEASE. (E.) Sharma, J. M. (Washington State U. Coll. Vet. Med., Pullman), S. G. Kenzy and A. Rissberger. J. Nat. Cancer Inst. 43(4):907-916, 1969.

The gamefowl classical isolate (WSU-GF) of Marek's disease virus (MDV), obtained from the kidneys of a chicken with clinical symptoms of the disease, had a CPE resembling that of Group B herpesviruses in chicken kidney (CK) cultures. The CPE was inhibited by 5-iodo-2'-deoxyuridine. After serial transfer of infected cells to CK cultures, the CPE was altered, with much larger polykaryocytes and more frequent Type A inclusions. Optimal expression of the CPE required a pH of 7.5 and an incub. temperature of 37°C (in CO₂). To obtain a max. number of foci of infection, the minimal contact time between the infected and normal CK cells was 12 hours. The cells became infectious before they became rounded and refractile.

- 70-508 LOCALIZATION OF VIRAL ANTIGEN IN CHICKENS INFECTED WITH MAREK'S DISEASE HERPESVIRUS. (E.) Calnek, B. W. (New York State Vet. Coll., Ithaca) and S. B. Hitchner. J. Nat. Cancer Inst. 43(4):935-949, 1969.

Gonadal tumor cells infected with Marek's disease virus (MDV; JM isolate), which was either contaminated with A-subgroup resistance-inducing factor virus (RIFV-A) or free of both RIFV-A and B-subgroup resistance-inducing factor virus (RIFV-B), were inoc. by several routes into chickens of 2 strains: a MDV-susceptible strain (S-line; derived from a flock of White Leghorns infected with RIFV-A) and a less susceptible strain (PDRC; free from most recognized avian

pathogens, including RIFV-A and RIFV-B). The MDV preparation free of RIFV-A and RIFV-B was less potent than the RIFV-A-contaminated preparation. MDV showed a predilection (determined by fluorescent antibody stain) for the medullary cells of the bursa of Fabricius and for a variety of epithelial cells (particularly in the kidney tubules and the feather follicles), but the lymphoid cells of MDV-induced neoplasms were infrequently stained. Factors affecting the number of positive tissues/bird and the extent of the MDV infection within the tissues (genetic susceptibility to MDV, age at inoc. and route of inoc.) were essentially the same as the factors influencing the incidence of the disease. Genetic constitution and the route of exposure also seemed to influence the rate of MDV infection.

- 70-509 ANTIBODIES TO EPSTEIN-BARR VIRUS IN BURKITT'S LYMPHOMA AND CONTROL GROUPS. (E.) Henle, G. (Children's Hosp. Philadelphia, Pa.), W. Henle, P. Clifford, V. Diehl, G. W. Kafuko, B. G. Kirya, G. Klein, R. H. Morrow, G. M. R. Munube, P. Pike, P. M. Tukei and J. L. Ziegler. J. Nat. Cancer Inst. 43(5):1147-1157, 1969.

Antibodies to Epstein-Barr virus (EBV) were found in sera from 139/139 East African children with Burkitt's lymphoma (BL). High titers (1:160 or over) were seen in 87%. Low titers (1:80 or less) were seen in a few pts. with histologically confirmed BL, but were somewhat more frequent among moribund pts., 3-yr. survivors and pts. with unconfirmed or doubtful BL. High anti-EBV titers, possibly reflecting recent EBV infections, were seen in only 14% of the sera from 489 children in several control groups (age-, sex- and tribe-matched; siblings or neighbors of BL pts.; normal children from regions of high or low BL incidence; randomly selected infants and children). Distribution of anti-EBV titers were about the same in all of these control groups, as well as in an adult control group (parents, older relatives and older neighbors of BL pts.) and a smaller group of pts. with other malignant or non-malignant diseases (including reticulum cell sarcoma, Hodgkin's disease and Kaposi's sarcoma). The geometric mean anti-EBV titer in the controls was 8-fold lower than in pts. with confirmed BL (1:326 in the BL pts.).

- 70-510 THE ASSOCIATION OF HERPESVIRUS TYPE 2 AND CARCINOMA OF THE UTERINE CERVIX. (E.) Rawls, W. E. (Baylor U. Coll. Med., Houston, Tex.), W. A. F. Tompkins and J. L. Melnick. Amer. J. Epidemiol. 89(5):547-554, 1969.

Sera from several groups of persons, predominantly Negroes of low socioeconomic status, were tested for antibodies to herpesvirus type 2 (HV-2). HV-2 antibodies were found in sera from 5/21

(24%) with dysplasia and 8/23 (35%) with carcinoma *in situ* of the cervix. In pts. with invasive (Stage I-IV) carcinoma of the cervix, the prevalence of HV-2 antibodies was 72% (42/65 pts.), including a prevalence of 64% (15/24 pts.) in a group of pts. successfully treated for invasive carcinoma of the cervix 4-20 yr. previously. HV-2 antibodies were also found in sera from 2/2 pts. with carcinoma of the vulva and 1 pt. each with carcinoma of the ovary and testicular seminoma, but sera from 18 pts. with other tumors (including carcinoma of the uterus, bladder and prostate) contained no HV-2 antibodies. In a control group of 266 persons, no HV-2 antibodies were found in sera from children under 12, and the prevalence of HV-2 antibodies among prostitutes (23/43 = 54%) was higher than in the controls (about 22%). It is concluded that HV-2 infection is spread venereally and is associated with carcinoma of the cervix, but a causative association between HV-2 and cervical cancer was not determined.

70-511 MAREK'S DISEASE HERPES VIRUS: A CYTOMEGALOVIRUS? (E.) Lee, L. F. (Dept. Microbiol., U. Chicago, Ill.), B. Roizman, P. G. Spear, E. D. Kieff, B. R. Burmester and K. Nazerian. *Proc. Nat. Acad. Sci. USA* 64(3): 952-956, 1969.

Purified MDV-DNA (KN variant of JM strain; grown on chick and duck embryo fibroblasts) had a buoyant density in CsCl corresponding to 56-57 moles guanine and cytosine per 100. The virus is not readily transmissible by cell-free filtrates. These properties are similar to those of herpes virus group B, which contains mainly cytomegaloviruses.

70-512 INDUCERS OF INTERFERON AND HOST RESISTANCE. VI. ANTIVIRAL EFFICACY OF POLY I:C IN ANIMAL MODELS. (E.) Nemes, M. M. (Merck Inst. Ther. Res., West Point, Pa.), A. A. Tytell, G. P. Lampson, A. K. Field and M. R. Hilleman. *Proc. Soc. Exp. Biol. Med.* 132(2): 776-783, 1969.

Admin. of polyriboinosinic:polyribocytidylic acid (poly I:C; admin. i.p.) had no antiviral effect in chicks infected (i.p. or by contact) with Marek's disease virus, and little or no effect in chicks inj. (wing web) with Rous sarcoma virus. The effects of poly I:C on several acute lytic virus diseases in mice suggested a highly complex mechanism of action, related to virus and drug dosage, time sequences and the number and spacing of the doses of poly I:C.

70-513 MORPHOLOGY OF A DISEASE WITH FEATURES OF MALIGNANT LYMPHOMA IN MARMOSETS AND OWL MONKEYS INOCULATED WITH *Herpesvirus saimiri*. (E.) Hunt, R. D. (Harvard Med. Sch., Southboro,

Mass.), L. V. Meléndez, N. W. King, C. E. Gilmore, M. D. Daniel, M. E. Williamson and T. C. Jones. *J. Nat. Cancer Inst.* 44(2):447-465, 1970.

Herpesvirus saimiri (originally recovered from squirrel monkey kidney tissue cultures) was inoc. i.m. into 27 cotton-topped marmosets (*Saguinus oedipus*) and 3 owl monkeys (*Aotus trivirgatus*). All animals, except those inoc. with heat-inactivated virus, died after 13-48 days with a malignant lymphoma-like disease. The animals showed marked reticulum cell invasion associated with organ replacement in a variety of tissues (regularly in the liver, kidney, spleen, lymph nodes and adrenals; sometimes in the lung, choroid plexus, salivary gland and testis). Some animals showed leukocytosis and lymphocytosis, with immature lymphocytes, lymphoblasts and reticulum cells in the peripheral blood. An unusual feature of this disease was necrosis of pre-existing tissues (liver, spleen, kidney, adrenal cortex, thymus, bone marrow and lymph nodes), which was seen in nearly all animals and was often not related to infiltrates of tumor cells.

70-514 THE MECHANISM OF VIRAL CARCINOGENESIS BY DNA MAMMALIAN VIRUSES, VI. A NEW CLASS OF VIRUS-SPECIFIC RNA MOLECULES IN CELLS TRANSFORMED BY GROUP C HUMAN ADENOVIRUSES. (E.) Fujinaga, K. (St. Louis U. Sch. Med., Mo.), M. Piña and M. Green. *Proc. Nat. Acad. Sci. USA* 64(11):255-262, 1969.

Each virus-specific RNA from rat embryo cells transformed by an adenovirus (AV) of Group C (types 2, 5 and 6) hybridized equally well with all viral DNA's of that group (types 1, 2, 5 and 6). No significant hybridization was seen between AV-2-specific RNA and DNA's of AV-12 (Group A), AV-7 (Group B), AV-4, -8 or -26, or *Pseudomonas aeruginosa*. Similar results were seen using RNA from AV-5-transformed cells. Thermal elution profiles of hybrids between AV-2-specific RNA and DNA's from all Group C AV's were identical. DNA-DNA homology measurements showed 83-93% common base sequences in the Group C AV's. Base composition analysis showed the guanine plus cytosine (G + C) content of AV-2-, AV-5- and AV-6-specific RNA's as 49%, 51% and 50%, resp. The G + C content of viral DNA from Group C AV's was 7-9% above this value, suggesting that it is not all transcribed.

70-515 GANGLIOSIDES IN DNA VIRUS-TRANSFORMED AND SPONTANEOUSLY TRANSFORMED TUMORIGENIC MOUSE CELL LINES. (E.) Mora, P. T. (NCI, Bethesda, Md.), R. O. Brady, R. M. Bradley and V. W. McFarland. *Proc. Nat. Acad. Sci. USA* 63(4):1290-1296, 1969.

In virally (SV40)-transformed cells, reduction in the highest ganglioside homologue, disialo-

ceramidetetrahexosamide was most pronounced, and monosialo-ceramidetetrahexosamide and total net ganglioside content were decreased to a lesser extent. Related to this decrease was an increased saturation density in tissue culture and the presence of cell surface transplantation antigens facilitating rejection when inj. into immunocompetent mice. This was a consistent finding in transformed cells with the viral genome, but was not seen in spontaneously transformed or normal cells.

70-516 TRANSFORMATION OF MOUSE L CELLS BY A VIRUS COMING FROM INVERTEBRATES: THE DENSONUCLEOSE VIRUS (VDN). (Fr.) Kurstak, E. (U. Montreal, Canada), S. Belloncik and C. Brailovsky. *C. R. Acad. Sci. [D] (Paris)* 269(17):1716-1719, 1969.

When mouse L cells (ATCC 929; C3H/AN) were infected with so-called densonucleose virus, a DNA virus derived from larvae of *Galleria mellonella* (Bee moth), followed by continued culturing and 2 passages per week, initial morphologic changes were in evidence by the third or fourth day and replication, which had been preceeding at a uniform rate, became anarchic. By the fifth day, many groups of round cells were seen, superposed on one another in heaps or piles, and such groups were reproducible, after cloning, without virus reinfection. Most of the cells showed evidence of transformation by the eighth day, with transformation antigens demonstrable by immunofluorescence in both the initially infected culture and cultures of cells which had undergone one or more passages. Although none of the transformed cells yielded infectious viral particles, they showed margination of the nuclear chromatin, similar to that which is observed following the *in vitro* infection of newborn Syrian hamster cells by SV40 virus.

70-517 TUMORS, HORMONES, AND VIRUSES IN *Drosophila*. (E.) Burdette, W. J. (U. Texas M. D. Anderson Hosp., Houston). *Nat. Cancer Inst. Monogr.* 31:303-321, 1969.

Effects of exposure to SV40 and to several strains of Rous sarcoma virus (RSV) were studied

in several stocks of *Drosophila*. Exposure to the Bryan strain of RSV (RSV-B) increased the incidence of melanotic tumors in larvae and pupae of the multipurpose and Oregon R stocks, but not in a strain with a higher spontaneous tumor incidence (tu 36a). SV40 increased the tumor incidence in the multipurpose stock. RSV-B often markedly increased the frequency of lethal mutations on the X chromosome, whereas the Schmidt-Ruppin and 559 strains (RSV-SR and RSV-559, resp.) had no significant effect. RSV-B was also more effective than RSV-SR and RSV-559 in increasing the numbers of chromosomal aberrations and nondisjunctions in the somatic and germ cells. Exposure to SV40, RSV-B, RSV-SR and the RAV-1 strain of RSV, reduced the mean size of chromosomal puffs at selected loci on the X and #3 chromosomes. It is suggested that both RNA and DNA viruses can alter the DNA template and interfere with messenger RNA synthesis in *Drosophila*.

70-518 ONCOGENIC EVALUATION IN HAMSTERS OF HUMAN PICORNA-, PARAMYXO-, AND HERPES-VIRUSES. (E.) Trentin, J. J. (Baylor Coll. Med., Houston, Tex.), G. L. Van Hoosier, Jr., D. B. Ferguson and I. Kitamura. *Proc. Soc. Exp. Biol. Med.* 132(3):912-915, 1969.

The oncogenic effects of 33 picornaviruses, 3 reoviruses, 6 paramyxoviruses and 1 herpesvirus (herpes simplex) of human origin, were studied in 1268 newborn hamsters. In a closed colony of hamsters, malignant tumors developed in 8/1671 (0.5%): 1 sarcoma, 3 lymphomas, 2 cheek pouch tumors and 2 carcinomas. Malignant tumors developed in 1 animal each (2.2-17% of each infected group) infected with echovirus types 12 (Travis 2-85 strain), 17 (CHHE-29 strain), 22 (Harris strain), 23 (Williamson strain) or 29 (JV-10 strain), respiratory syncytial virus (Long strain) and reovirus type 3 (Abney strain). The tumors in the echovirus type 12 and reovirus groups were malignant lymphomas; the other tumors were either sarcomas or unclassified, highly autolytic tumors resembling sarcomas. No carcinomas or cheek pouch tumors were seen in the infected animals. The possible roles of contaminating oncogenic viruses (especially SV40 contamination of the echoviruses), or enhancement or activation of enzootic latent viruses by the non-oncogenic viruses, are discussed.

See also abstract nos.: 357,408,523,554

70-519 TECHNICAL, CLINICAL AND EPIDEMIOLOGIC DRAWBACKS TO THE EARLY DIAGNOSIS OF CARCINOMA OF THE CERVIX. (It.) Bertone, C. (Oncol. Inst., Turin, Italy), A. Salvati, P. L. Ponte and D. Semeraro. Cancro 21(4):395-411, 1968.

Among 10,000 pts. undergoing colposcopy for suspected cervical carcinoma, 39% were referred for histologic study of suspect lesions, and preclinical cancer was demonstrated in 11%. Among 4650 lesions rated benign by colposcopy, 0.3% proved cytologically positive (Papanicolaou technique), 16.0% were cytologically suspect. Among 3,350 rated suspect by colposcopy, 24.5% were cytologically suspect; 2.7% were true positives, 0.19% were false positives, and 0.10% were false negatives as concerned the Papanicolaou findings, when confirmed histologically. Among the cases reported as cytologically suspect, only 0.5% were histologically positive. The Papanicolaou technique yielded 94.1% true and 5.9% false positives. Karyologic studies of lesions rated benign by colposcopy yielded 90.8% negative, 9.0% suspect, and 0.1% (each) true and false positive. The false positive and suspect lesions all involved severe inflammatory conditions. The true positives were all endocervical carcinomas. Karyologic studies of lesions rated suspect by colposcopy yielded 89.2% negative, 7.0% suspect, 3.1% true and 0.5% false positive, with 0.2% false negative as confirmed by histologic examination. This technique yielded 96.8% true and 3.2% false positives. Among all pts. in whom cervical carcinomas were demonstrated, 33% were still in a preclinical stage, 32% had already suffered initial invasion, and the cancer was firmly established in 35%.

70-520 ANALYSIS OF ENVIRONMENTAL FACTORS IN PATIENTS WITH UTERINE CERVIX AND CORPUS CANCER. (Pol.) Sablińska, B. (Inst. Oncol., Warsaw) and B. Nozdryn-Piotnicki. Ginek. Pol. 40(11):1245-1250, 1969.

Statistically significant differences were detected between 980 pts. with cervical and 318 with uterine corpus cancer treated between 1960 and 1966. The largest percentage of pts. with cervical cancer was in the sixth, with corpus cancer in the seventh decade of life; 52.2% of the former, 88.8% of the latter were less than 50 yr. old. In both groups the largest percentage (46.4% and 42.5%, resp.) lived in rural areas or small towns, the smallest in large cities (3.1% and 6.2%, resp.) while 27.6% and 27.7%, resp., lived in Warsaw. Of cervical cancer pts. 54.5% came from a blue collar background, 21.4% from a higher educational (socio-economic) background; the corresponding figures for those with corpus cancer were 43.1% and 34.6%, resp. Including retired pts., 50.5% of the first group were physical workers, 37% without occupation, in the

second 37.7% were physical workers and 43.4% without occupation. Significantly fewer white collar and professional workers were found in the former (12.5%) than latter group (18.9%). Only 3.7% of those with cervical cancer were never pregnant as opposed to 14.4% of those with corpus cancer, 74.5% of the former and 53.8% of the latter had 3-10 pregnancies, but contrary to previous reports the percentage of those with 3-5 pregnancies in the latter group was high (39.0%).

70-521 CORRELATION BETWEEN CHRONIC AND MALIGNANT DISEASES OF THE PANCREAS. (Ger.) Grözinger, K.-H. (U. Heidelberg Path. Inst., Germany), F. Dallenbach and H. Heisler. Langenbecks Arch. Klin. Chir. 326(1):47-61, 1969.

Among 167,970 pts. hospitalized between 1943-1966 cancer of the pancreas was diagnosed in 169 (0.1%) (110 men, 59 women). Of female pts. 66%, and of male pts. 62% were 51-70 yr. old. Diagnosis was confirmed histo-pathologically in 77 cases (38 biopsy, 39 autopsy) and at surgery in 92 cases. The most frequent localization was the head of the pancreas, invasive growth was observed in 56 pts. metastases in 104. In 77% of pts. the tumors originated in the pancreatic ducts, adenocarcinoma was present in 56/77, poorly differentiated carcinoma in 9/77. Chronic inflammatory changes coexisted with carcinoma in 33/57 (57.9%) of evaluated cases. In 19 cases carcinoma was probably the result of these chronic lesions indicating an etiologic-pathogenic relationship between chronic and malignant pancreas diseases in 33% of histologically confirmed cases. It is suggested that carcinoma was the consequence and not the cause of fibrotic changes in the majority of pts. with tumor and fibrosis. It is suggested that chronic diseases of neighboring organs do not contribute to tumor formation in the pancreas.

70-522 PRIMARY CANCER OF THE LIVER IN BULGARIA. (Ger.) Kantshev, K. (State Hosp. Burgas, Bulgaria). Z. Ges. Inn. Med. 24(20): 699-702, 1969.

In contrast to West European countries the incidence in Bulgaria is high: it averaged 0.62% of reported autopsies and constituted 8.5% of all autopsied carcinomas. An especially high incidence was noted in the south-eastern part of the country (Burgas area). Over a 20-yr. period (1945-1965) 94 autoptically confirmed cases which constituted 1.38% of all autopsies and 19.3% of carcinomas were observed. The majority were men (84) and most (83%) were in the fifth to seventh decade of life, only 6 were less than 40 yr. old. In 64.8% it was accompanied by liver cirrhosis (all except one of the atrophic type). Symptoms, laboratory findings and

clinical picture of the cirrhotic and hepatomegalic forms of primary liver cancer are described and possible etiologic factors discussed. Echinococcus alveolaris hepatitis was present in 2/94 and a definite nutritional imbalance existed in 13/94 (17.02%).

- 70-523 ANTIBODIES TO EPSTEIN-BARR VIRUS IN NASOPHARYNGEAL CARCINOMA, OTHER HEAD AND NECK NEOPLASMS, AND CONTROL GROUPS. (E.) Henle, W. (U. Pennsylvania Sch. Med., Philadelphia), G. Henle, H.-C. Ho, P. Burtin, Y. Cachin, P. Clifford, A. de Schryver, G. de-Thé, V. Diehl and G. Klein. J. Nat. Cancer Inst. 44(1):225-231, 1970.

In sera from 235 East African and Chinese (Hong Kong) pts. with carcinoma of the nasopharynx (NPC), the geometric mean titer of Epstein-Barr virus (EBV) antibodies was 1:348; high titers (1:160 or higher) were seen in 84% of these pts., irrespective of tumor histology. In untreated Chinese pts. with NPC, the geometric mean titers increased from 1:103 in Stage I to 1:788 in Stage V, and the frequencies of high titers increased from 45% to 100%. In 6 French pts. with NPC, the geometric mean EBV antibody titer was 1:61, and 3/6 showed high titers. Geometric mean EBV antibody titers in 185 pts. (from East Africa, Hong Kong, India and France) with head and neck tumors (usually carcinomas) other than NPC, in 52 pts. with tumors other than carcinomas, and in 237 control subjects (from East Africa, Hong Kong and India), were 1:36, 1:43 and 1:37, resp., and high titers were seen in 13.0%, 13.5% and 11.4%, resp. No explanation could be offered for the apparent association of EBV with NPC, but not with other head and neck carcinomas.

- 70-524 EPIDEMIOLOGY OF LYMPHOGRANULOMATOSIS (HODGKIN'S DISEASE). (Ger.) Dörken, H. (U. Hamburg Med. Clin., Germany). Deutsch. Med. Wschr. 94(13):666-670, 1969.

The raw and standardized mortality rates (per 100,000/yr.) from different European countries (World Health Organization 1958) were compared to those from Lower Saxony, Schleswig Holstein and Hamburg (based on examination of 272,000 death certificates in 1964-1965). Norway had the lowest standardized rates for males (1.4), Hungary the lowest for females (0.8); Czechoslovakia had the highest for males (3.2), West Berlin the highest for females (2.1). The rates for Lower Saxony were 1.6 and 1.4, for Schleswig Holstein 2.0 and 1.5, resp., for Hamburg 2.2 and 1.6, resp. (standardized). Of non-European countries Ceylon and Japan had the lowest (0.1 and 0.8 for males and 0.1 and 0.4 for females, resp.), USA (white) and Union of South Africa (white) the highest (2.4 and 2.5 for males, 1.6 and 1.5 for females, resp.). In all countries with the exception of Norway and North Ireland the rates were lower for women than men. Low mortality

rates (raw) have also been reported (1961) for Hong-Kong (0.2-0.1), Singapore (0.2-0.1), Dominican Republic (0.0-0.1) and Egypt (0.0-0.1). High standardized morbidity rates for males were reported for Columbia (3.7), Puerto-Rico (3.5) and Jamaica (3.3), while those for females in Jamaica were low (0.3). High morbidity rates among children (under 15 yr.) were observed in Peru (40.7% of patients) and Lebanon (22.45%). Race differences were also noted: mortality rates were lower for non-white populations in New Zealand, South Africa and USA and twice as high among Jews > 40 yr. old in Brooklyn, New York.

- 70-525 SEASONAL VARIATIONS IN ONSET OF LYMPHOGRANULOMATOSIS. (Ger.) Uhl, N. (U. Göttingen, Germany) and W. Hunstein. Arch. Klin. Med. 216(4):355-370, 1969.

Analysis of the age distribution of 315 pts. (60.5% males, 39.5% females) with Hodgkin's disease revealed a biphasic curve; one peak of incidence between 16-35 yr. (mostly females), the other between 50-65 yr. (mostly males). The acute, rapidly progressing form was seen predominantly in the older age group (1/5 of pts.). Determination of mo. of onset of first symptoms (229 pts.) showed a lower than expected (8.3%) frequency between April (6.1%) and August (4.4%), with a minimum in July (1.8%), and a sharp increase between September (9.2%) and March (12.7) with a peak in January (14%). The first hospitalization showed a similar seasonal rhythm with a lag of 1-2 mo. after first manifestations. Onset of recurrences also showed a seasonal rhythm with a peak in the fall (October) and lowest point during the summer. Possible causes for these seasonal fluctuations such as viral infections, resistance and biological rhythm of pts. are discussed.

- 70-526 STATISTICAL RELATIONSHIP BETWEEN SMOKING AND BRONCHIAL CARCINOMA IN AUTOPSY MATERIAL. (Ger.) Möbius, G. (Path. Inst., Schwerin, Germany), H. Zschoch and K. Springfield. Deutsch. Gesundh. 24(51):2426-2430, 1969.

Catamnestic (questionnaire) analysis of 1001/2016 (895 men, 106 women) bronchial carcinoma autopsy cases from the pathological institutes at Leipzig (2), Schwerin and Greifswald, Germany (1958-1963) revealed that 96.3% of male and 19.8% of females had been smokers as opposed to 53.4% of male and 8% of females in the living population at large (according to a study by Werner). While the majority (65.1%) of the living smoked cigarettes and only 8.2% were mixed (cigarettes, pipe, cigars) smokers, the greatest percentage (44.7%) of autopsy cases had been mixed smokers (35.1% smoked only cigarettes, 20.0% pipe and/or cigars). The majority of the mixed smokers (53.1%-58.5%) were extremely heavy smokers (21 - more than 35 cigarettes/day), the

majority (55.9-60.5%) of cigarette smokers smoked less than 21/day. While of the living male population only 38.8% smoked more 10 cigarettes/day, 91.7% of the autopsied bronchial carcinoma males smoked more than 10 cigarettes/day.

70-527 GEOGRAPHIC PATHOLOGY OF BRONCHIAL CARCINOMA IN EAST GERMANY. (Ger.) Zschoch, H. (Path. Inst., Brandenburg, Germany), G Möbius and K. Springfield. Deutsch. Gesundh. 24(51):2420-2426, 1969.

Comparison of autopsy records from 2 pathological institutes in Leipzig (industrial area) with 2 in the northern agricultural area of East Germany (Schwerin and Greifswald) revealed a higher incidence in the former: 10.0% of male 1.4% of female as compared to 6.4% and 0.9%, resp., in Schwerin and 7.8% and 1.6%, resp., in Greifswald. The greatest frequency among males was in the 61-70 yr. age group (12.6%). Between 1951-1960 neoplasms constituted 24.3% and 25.6% of all autopsies in Leipzig, 21.4% in Schwerin and 26.2% in Greifswald. Bronchial carcinomas were the most frequent of all neoplasms (9.5%, 8.9% in Leipzig, 6.4% in Schwerin and 7.8% in Greifswald). Prevalence of females among the living population in the Leipzig area underlined the higher rate of bronchial carcinoma among males. The statistical difference of these findings was not influenced by migration of the population, age distribution and composition of autopsy and tumor cases or age composition of the living population. It is suggested that air pollution was an additional causal factor.

0-528 NEOPLASMS OF THE UPPER PART OF THE DIGESTIVE AND UPPER RESPIRATORY TRACT IN THE CLINICAL MATERIAL OF THE INSTITUTE OF ONCOLOGY IN CRACOW. (Pol.) Skolyszewski, J. (Inst. Oncol., Cracow), M. Pawlicki and A. Brzdanowski. Otolaryng. Pol. 23(5):525-529, 1969.

Neoplasms of the lip, oral cavity, pharynx and larynx constitute a much larger percentage of all malignancies in the Cracow area (5.7%) than in other countries: Denmark 2.6%, Sweden 2.5%, USA 1.7%. Between 1951-1960 (inclusive) 2,028 cases (2.2% of all neoplasms) were seen at the outpatient clinic of the Oncological Institute in Cracow, Poland. These included: neoplasms of the lip 7.6%, oral cavity 1.2%, pharynx 1.1%, and larynx 2.3%.

-529 LUNG CANCER MORTALITY INCREASE IN POLAND. (Pol.) Staszewski, J. (Inst. Oncol., Gliwice, Poland). Nowotwory 19(4): 3-267, 1969.

Between 1959-1967 the age-adjusted lung cancer mortality rates (per 100,000) increased 116% among males (75% in urban, 224% in rural areas)

and 48% among females (14% in urban and 107% in rural areas). The rates increased faster in rural than in urban areas (especially among the above 65 age groups) causing a decrease in urban/rural ratio from 3.4:1 in 1959 to 1.9:1 in 1967 for males and from 2.7:1 to 1.5:1 in females. The male:female sex ratio increased during that time from 4.8:1 to 6.8:1. Analysis of age-adjusted rates and percent increase of crude lung cancer mortality rates according to regions show a sharper increase in eastern rural areas where they were low originally, but might be partly due to improved reporting and diagnosis in these regions. Although in 1967 lung cancer mortality rates for males were 20% lower than those for stomach cancer, lung cancer is now the leading cause of cancer deaths in urban areas and second (after stomach cancer) in rural areas. It is concluded that since both cigarette consumption and lung cancer mortality rates are increasing a continued rise in lung cancer incidence can be expected in Poland.

70-530 EPIDEMIOLOGY OF CARCINOMA. I. AN INVESTIGATION BASED ON STATISTICAL DATA FROM ISRAEL. (Ger.) Kallner, G. Med. Welt 20(17):1006-1012, 1969.

Part I is an introduction to the translated (from English) abridged version of the WHO/CANC/66.68, Part I & II report (a retrograde investigation). It deals with the rationale for this study (comparison of incidence in different immigrant groups) and description of material: mortality data for 1950-1954 ("first mortality period") (5838 cases) and for 1958-1961 (second mortality period) (7433 cases) and cancer morbidity data: 16,000 cases comprising 80-85% of all cancer cases in Israel. Possible shortcomings of methods are discussed.

70-531 EARLY DETECTION OF CANCER BY THE GENERAL PRACTITIONER AND THROUGH LARGE SCALE EXAMINATIONS. (Ger.) Muggler-Bickel, J. (U. Zurich Inst. Soc. Prev. Med.). Therap. Umsch. 26(10):604-608, 1969.

About 20% of all deaths in Switzerland (11,000 of 56,000/yr.) are due to neoplasms. Of 6013 men who died of cancer in 1966 about 24% were less than 60 yr. old (146 less than 30, 93 were in the fourth, 267 in fifth, 975 in sixth, 1892 in the seventh, 1815 in the eighth decade and 825 were less than 80 yr. old). The corresponding figures for women were: 101, 104, 301, 781, 1415, 1520 and 914. Early deaths (< 60 yr. old) were most frequently seen in Hodgkin's disease, leukemia, skin cancer and uterine cancer. Among men the most frequent cancers in Switzerland are: (in descending order) lung and bronchii, stomach and prostate, among women breast, stomach and genital organs. In general practice early detection is possible (by simple inspection, palpation or cytology) in superficially located

carcinomas such as breast, uterus, skin and rectum. Early detection constitutes secondary prophylaxis (primary-avoidance of carcinogenic factors) and is possible in cancer of prostate, skin, breast, cervix, rectum and, to a lesser extent, lungs and uterine body. Purposeful large scale examinations are recommended mainly for population groups with a higher than average incidence of a certain type of cancer. From a social point of view it is more important to use the available facilities for detection and treatment of 30-60-yr.-old pts. than for age-dependent diseases of those under 70 yr. of age. During examinations it is senseless to elaborately search for very rare tumors or needlessly subject young people to such examinations.

70-532 EPIDEMIOLOGY OF CANCER OF THE BREAST, STOMACH, ESOPHAGUS, LUNGS, BLADDER AND HODGKINS DISEASE. (Ger.) Heyden, S. (Duke U. Med. Ctr., Durham, N. C.). Deutsch. Med. J. 20(1):3-9, 1969.

A review and discussion. Every factor which contributes to lowering of estrogen levels decreases the risk of breast cancer in women. In Japan where women have many children and usually nurse them for long periods of time the incidence of breast cancer is one-ninth that in the West. The extremely high incidence of stomach cancer in Tyrol (Austria) and Poland is attributed to consumption of large quantities of lard, the high incidence in Japan (fat-poor diet) to malignant transformation of stomach ulcers which are common in that country. Different etiologic factors are responsible for tumors in different segments of the same organ (for inst. uterine cervix and corpus cancer): high incidence of esophagus carcinoma (upper third of the esophagus) in Sweden was attributed to a lack of iron and sideropenia, while the extremely frequent esophagus cancer among the Bantu in South Africa who have a very high blood iron level, is localized in the thoracic part of the esophagus. Different histology of neoplasms in the same organ can also be an expression of different etiologic factors. The dependence of cancer of the bladder on occupational factors is well established, but smoking also seems to be a causative factor. Hodgkins disease is almost unknown in people less than 50 yr. old in Japan, but in older age groups its frequency is as high as in Europe or the USA.

70-533 A STUDY OF FAMILIAL INCIDENCE OF CUTANEOUS MELANOMAS. (It.) Tosoni Dalai, M. I. (U. Milan Inst. Human Genet., Italy), M. G. Ronzoni Bernardi and P. L. Meneghelli. Tumori 55(3):161-166, 1969.

An inquiry into the family histories of 122 pts. with cutaneous melanomas which had been confirmed histologically showed an increased familial incidence of neoplastic disorders in general, as

compared to 122 controls who were matched for age and social-economic status. Differences were statistically significant for 3 categories: the mother, brothers and sisters. For the father, the differences shown were just below the level of statistical significance. For offspring, a lack of sufficient offspring among the control subjects made reliable comparison impossible. There was no apparent correlation with any particular tumor site among the affected members of the family.

70-534 EPIZOOTIOLOGY OF PAPILOMAS IN ENGLISH SOLE, Parophrys vetulus. (E.) Cooper, R. C. (U. California Sch. Pub. Health, Berkeley) and C. A. Keller. Nat. Cancer Inst. Monogr. 31:173-185, 1969.

Papillomas were found in 12% of 15,739 English sole (Parophrys vetulus) collected in San Francisco Bay from September, 1965-September, 1966. The tumor frequency varied from 3-28% in fish collected at different times and places, with a peak frequency in May-September. Since the tumors were distributed approx. randomly on the body surfaces, it is suggested that the tendency to develop tumors may begin before metamorphosis. Tumor-bearing fish resembled normal fish in many respects, but apparently showed significant differences in the growth rate (which could not be attributed directly to a debilitating effect of the tumor on the host) and the time of birth. No such tumors were noted in flatfish of any of the other species (about 7) collected from San Francisco Bay. The possible role of a monogene trematode (Gyrodactilus sp.), an ectoparasite found only on the English sole, is mentioned. Tumor-bearing fish were about twice as frequent in the North Bay as in the South Bay throughout the study period. The North Bay is shallower, with a larger fresh water inflow and more direct influence by industrial pollution (especially petrochemicals), than the South Bay. The possible existence of 2 populations of English sole in San Francisco Bay, differing from each other in either genetic factors or in exposure to environmental factors, is suggested.

70-535 BRONCHIAL CARCINOMA IN WOMEN. (Pol.) Wiczorkiewicz, A. (Inst. Oncol., Gliwice, Poland) and F. Witkowski. Nowotwory 19(4):275-278, 1969.

Between 1947-1961 (inclusive) 159 women and 1621 men were seen at the Oncologic Institute in Gliwice, Poland, for suspected bronchial carcinoma. Histopathological verification was obtained in 652 men and 159 women (almost 15:1 ratio). Differences in microscopic structure of tumors in males and females were noted. Small cell carcinoma and adenocarcinoma occurred more frequently in females (28.9% and 26.7%, resp.) than in males (17.0% and 5.2%, resp.).

The incidence of squamous cell carcinoma was 20.0% in females, 38.8% in males, solid carcinoma 11.1% and 18.6, resp., and unclassified 13.3% and 20.4%, resp. A relatively large number of women were young: 8.9% were 21-30, 8.9% were 31-40, 22.2% 41-50, 33.3% were 51-60, 24.5% were 61-70 and 2.2% more than 70-yr.-old.

70-536 PROLIFERATION CHARACTERISTICS OF THE VARIOUS CLASSES OF CELLS IN HODGKIN'S DISEASE. (E.) Peckham, M. J. (Roy. Marsden Hosp. Inst. Cancer Res., Surrey, England) and E. H. Cooper. Cancer 24(1):135-146, 1969.

Fresh lymph node material was obtained by surgical excision from 10 pts. with Hodgkin's disease. The cell population consisted of normal reticulum cells, abnormal reticulum cells (Hodgkin's cells), transformed lymphocytes, and medium and small sized proliferating lymphoid cells. The majority of transformed lymphocytes and the outer lymphoid cells had DNA values within normal limits. However, considerable aneuploidy was seen in the abnormal reticulum cells. These had a lower tritiated thymidine labelling index than transformed lymphocytes. No evidence of DNA synthesis was seen in Sternberg-Reed cells.

0-537 GROWTH REGULATION AND CARCINOGENESIS IN THE EPIDERMIS OF MICE. (Ger.) Versen, O. H. (U. Oslo Inst. Gen. Exp. Path.). Arch. Geschwulstforsch. 32(4):322-338, 1968.

Growth regulation as a complicated interplay of stimulants, inhibitors and modulators is discussed in the framework of cybernetics with special emphasis on the "feed back" mechanism. Experiments on the kinetics of cell populations and growth regulation in the epidermis of hairless mice are reviewed and the use of an experimental model for study of epidermal growth kinetics described. Painting with 1% methyl-nolanthrene causes an immediate cell damage (disturbance of energy production) resulting in an immediate blocking of cell renewal. This is then followed by sharply increased cell regeneration (3 times normal 1 day after application) and gradual return to normal by the fifth day. Hence there is a simultaneous increase in cell destruction during the first 2 days, hyperplasia develops on the third day. In the epidermal feed-back mechanism an epidermal chalone is the locally acting, growth controlling substance. It is probably a macromolecule (molecular wt. 40,000), a protein or glycoprotein with anti-tumour characteristics, stable at low pH and isoelectric point between 5 and 6. Chalone is tissue-specific but not species-specific. Different theories of disturbed growth regulation and carcinogenesis from a cybernetic viewpoint are presented.

-538 EARLY PHASES IN THE DEVELOPMENT OF BREAST CANCER. (E.) Gallager, H. S.

(U. Texas M. D. Anderson Hosp., Houston) and J. E. Martin. Cancer 24(6):1170-1178, 1969.

Correlations between mammographic and pathological findings were studied in 112 mastectomy specimens of primary (55) or metastatic (3) carcinomas, cystosarcoma phylloides (1) or fibrocystic disease (1) of the breast. The results showed that the carcinoma affects both the epithelial tissues (diffusely, not focally) and the supporting connective tissue. The earliest histologically recognizable stage in the sequence leading to invasive carcinoma is epithelial hyperplasia of the mammary ducts and lobules (regarded as a non-obligate preneoplastic lesion). Infiltrating carcinomas are preceded by intraepithelial non-invasive carcinomas. Carcinomas *in situ* commonly show concurrent invasion at multiple sites. The tumor may spread by the formation of new invasive nodules from intraductal carcinomas, and/or by local lymphatic extension. Configurations of invasive carcinomas may reflect their growth rates.

70-539 DATA ON THE GROWTH RATE OF HUMAN TUMORS. (Fr.) Rambert, P., E. Malaise, A. Laugier, M. Schlienger and M. Tubiana. Bull. Cancer (Paris) 55(3):323-341, 1968.

In 56 children and adults with single or multiple metastases to the lungs (30/56), s.c. tissues (2/56) or lymph nodes (23/56) from a wide variety of tumors, tumor growth rates were exponential in most pts., although 11 metastases showed an important reduction of the tumor doubling time during the observation period. Tumors of similar histology showed wide variations in the doubling time (in pts. with lung metastases, doubling times were: 14-66 days in 12 osteosarcomas; 9-130 days in 3 soft tissue sarcomas; 10-45 days in 5 testicular dysembryomas; 10-30 days in 3 hematosarcomas; 20-690 days in 4 thyroid carcinomas). In some pts. with multiple measurable tumors, the doubling times varied widely from 1 tumor to another.

70-540 CONTRIBUTIONS TO THE STUDY OF THE CELL PATHOLOGIC MORPHOLOGY IN ACUTE LEUKEMIA. NOTE IV. BIOSTATISTIC VARIATIONS OF THE CELL SIZE PARAMETERS. (E.) Niculescu, M. I. (Acad. Soc. Rep. Rumania Inst. Med. Res., Cluj), M. Mihoc, I. Păvăloiu, L. Săceleanu and V. D. Mărza. Rev. Roum. Embryol. Cytol. 5(2): 83-102, 1968.

In bone marrow lymphoblasts and myeloblasts from 6 pts. with acute myeloblastic (AML; 4/6) or lymphoblastic (ALL; 2/6) leukemia, mean values for cellular, nuclear and cytoplasmic area, and the mean nuclear/cytoplasmic (N/C) ratios, were smaller than in bone marrow lymphoblasts and myeloblasts from 2 normal subjects. Cells from the pts. with ALL showed smaller mean values for nuclear and cytoplasmic area and a higher N/C ratio, than the cells from pts. with AML. The

distribution curves for these parameters of cell size were skewed to the right in the preparations from the leukemic pts. (the larger cells may have been aneuploid), but not in the control preparations. The variation coefficients of the N/C ratio among leukemic cells of similar nuclear area, suggested the presence of a minor cell population of nearly normal size; this finding was interpreted as favoring the theory of clonal evolution in acute leukemia.

- 70-541 A GENETIC RELATIONSHIP BETWEEN DIABETES AND CANCER. (E.) Kessler, I. I. (Johns Hopkins U. Sch. Hyg. Pub. Health, Baltimore, Md.). Lancet 1(7640):218-220, 1970.

The frequency of cancer was determined in 21,447 male and female diabetes mellitus pts. seen over 26 yr. Total cancer mortality occurred at normal frequency in females, but incidence among males was reduced about 15% from the normal population. Lung cancer was especially infrequent among male diabetics. A higher no. of the diabetic population (17%) was Jewish, than in the normal population (5%). The authors suggest a possible X-linked recessive genetic trait linked also with glucose-6-phosphate dehydrogenase variants, in which increased susceptibility to diabetes mellitus is associated with decreased susceptibility to cancer. A model is presented.

- 70-542 SMOKING AND CANCER OF THE ALIMENTARY TRACT IN POLAND. (E.) Staszewski, J. (Inst. Oncol., Gliwice, Poland). Brit. J. Cancer 23(2):247-253, 1969.

A retrospective study was made during 1957-59 and 1960-68 of 81 males and 7 females with carcinoma of the esophagus, 450 males and 178 females with carcinoma of the stomach and 240 males and 198 females with carcinoma of the large bowel. Controls were 771 males and 383 females hospitalized with disorders thought not to be associated with smoking habits. In males with carcinoma of the esophagus and stomach there was a significantly higher tobacco consumption than in controls. Results in females did not differ significantly from controls. For males, relative risk of male smokers vs. nonsmoker for carcinoma of the stomach was 1:6. When carcinoma of the stomach was classified by location in the stomach, male pts. with carcinoma of the cardia and carcinoma of the pyloric region had significantly higher smoking indices while pts. with carcinoma of the middle portion or whole of the stomach did not differ significantly from controls in their smoking habits. Females with carcinoma of

the cardia also differed significantly from controls in having a higher tobacco consumption.

- 70-543 FAMILIAL MULTICENTRIC FIBROMATOSIS - DESMOIDS. A REPORT OF THREE CASES IN A JORDANIAN FAMILY. (E.) Zayid, I. (Army Base Hosp., Amman, Jordan) and C. Dihmis. Cancer 24(4):786-795, 1969.

Desmoid tumors were reported in the mother (age 35) at the site of a cholecystectomy scar, in a son (age 22) associated with an appendectomy scar, and in a daughter (age 20) who had no history of trauma, pregnancy or surgery. Initial and/or recurrent tumors occurred within and outside the abdominal wall. Previous instances of familial incidence of desmoids were associated with Gardner's syndrome. This family had no history of familial polyposis, colonic cancer or desmoids other than the 3 reported cases. It is suggested that a genetic etiology is possible, presumably due to an autosomal dominant gene. Other etiological factors as various types of trauma and hormonal influences are discussed.

- 70-544 EPIDEMIOLOGY AND ETIOLOGY OF HUMAN BLADDER CANCER: OCCUPATIONAL BLADDER CANCER IN THE BRITISH RUBBER INDUSTRY. (E.) Parkes, H. G. (British Rubber Mfg. Ass. Health Res. Unit., Birmingham, England). J. Nat. Cancer Inst. 43(1):249-252, 1969.

A summary of the British rubber industry's efforts to reduce the incidence of bladder tumors among its workers and its contribution to the study of the epidemiology of bladder cancer. A permanent Industry Health Advisory Committee has been established to monitor prevalence and incidence of diseases of special interest.

- 70-545 INDUSTRIAL BLADDER CANCER: A PROGRESS REPORT AND SOME UNANSWERED QUESTIONS. (E.) Ferber, K. H. (Allied Chem. Corp., Buffalo, N. Y.). J. Nat. Cancer Inst. 43(1):245-248, 1969. Preventive measures taken by industry to reduce the exposure to possible carcinogens responsible for bladder carcinoma include cessation of manufacture (2-naphthylamine) and control of type of manufacturing process to prevent inhalation or skin absorption (benzidine). Some basic problems such as quantifying carcinogenic potency of chemicals, of determining dose effects of various carcinogens and their alteration of cell metabolism, still remain. A reliable screening test for bladder cancer is still not available.

See also abstract nos.: 355,509,510,550,551

70-546 COMPARATIVE EFFECTS OF TUMOR EXTRACTS ON LYMPHOCYTE TRANSFORMATION IN PERIPHERAL BLOOD CULTURES OF HEALTHY PERSONS AND PATIENTS WITH BREAST CANCER. (E.) Fischer, P. (Univ. Gynecol. Clin., Vienna), E. Golub, H. Holzner and E. Kunze-MUhl. Z. Krebsforsch. 72(2):155-161, 1969.

Peripheral blood lymphocytes from 12 pts. with breast cancer and 20 healthy male and female subjects were cultivated for 120 hr. in the presence of cell-free extracts from scirrhous breast carcinoma, with and without additional phytohemagglutinin (PHA; 0.1 ml). No significant difference in the degree of transformation (blast cells) was seen in cultures from the pts. and healthy controls (male and female) in the presence of PHA (9/12 pts., 15/20 controls). However, when the tumor extract alone was added and PHA omitted, a significantly greater frequency of lymphocyte transformation was observed in cultures from the pts. (8/12 pts., 4/20 controls). The implications of these findings for assessing the immunological reactivity of lymphocytes towards tumor antigens in malignant diseases are discussed.

70-547 ACUTE CHILDHOOD LEUKAEMIA IN RELATION TO THE HL-A HUMAN TRANSPLANTATION GENES. (E.) Walford, R. L. (U. California Los Angeles Med. Ctr.), S. Finkelstein, R. Neerhout, P. Konrad and E. Shanbrom. Nature (London) 225(5231):461-462, 1970.

In a study of 10 families with 1 leukemic child each and other sibling(s) available for HL-A typing (23 children; 20 parents), all 10 leukemics were HL-A1 negative; 9/10 were phenotypically Merritt positive; and 7/10 were HL-A 2 positive. The authors suggest that the presence of an HL-A Merritt haplotype may indicate an increased susceptibility to leukemia, but not an absolute susceptibility since some healthy parents and siblings of the leukemics studied also possessed the HL-A 2 Merritt haplotype.

70-548 THE STROMAL THECA CELL AND POST-MENOPAUSAL ENDOMETRIAL ADENOCARCINOMA. (E.) Fienberg, R. (Beverly Hosp., Mass.). Cancer 24(1):32-38, 1969.

Stromal thecal cells were found in the ovaries of 10/11 confirmed cases of postmenopausal endometrial adenocarcinoma, and studied by the use of a lipid stain and oxidative enzyme technique. The author concluded that in postmenopausal endometrial carcinoma attention should be directed to the stromal thecal cells rather than to the ovarian stromal hyperplasia.

70-549 ISOACCEPTING TRANSFER RNA'S OF L-M CELLS IN CULTURE AND AFTER TUMOR

INDUCTION IN C₃H MICE. (E.) Yang, W.-K. (Oak Ridge Nat. Lab., Tenn.), A. Hellman, D. H. Martin, K. B. Hellman and G. D. Novelli. Proc. Nat. Acad. Sci. USA 64(4):1411-1418, 1969.

When co-chromatography (in a reversed phase column) was performed on L-M cells from serum-free suspension cultures and on L-M cells from induced tumors, significant differences were seen in the chromatographic patterns of aspartyl-, histidyl-, phenylalanyl-, and tyrosyl-tRNA's as well as in alanyl-, isoleucyl-, seryl-, and threonyl-tRNA of the isoaccepting series. The patterns of arginyl-, methionyl-, prolyl-, tryptophanyl-, valyl-, glycyl-, leucyl-, and lysyl-tRNA were similar in both groups. Similar results were obtained whether the synthetases used were from cultivated cells or from tumors. Reculturing of tumor cells caused a reversion of tRNA patterns to that form. It is thought this represents an adaptation to nutritional change as addition of serum to the culture caused the appearance of small amounts of isoaccepting tRNA's, like those seen in tumor cells. Suggested mechanisms are that the different isoaccepting tRNA: (1) are gene products of the selected clones, (2) are induced by action of a foreign genome (viral), (3) are related to the expression of different gene functions.

70-550 HEREDITARY BLOOD AND SERUM TYPES, PTC TEST AND LEVEL OF THE FIFTH FRACTION OF SERUM LACTATEDEHYDROGENASE IN FEMALES WITH GYNECOLOGICAL CANCER. (I. COMMUNICATION). (E.) Miluničová, A. (Charles U., Prague), A. Jandová, L. Laurová, J. Novotná and V. Škoda. Neoplasma (Bratisl.) 16(3):303-309, 1969.

No increase in the incidence of blood group A was observed in a series of 291 women with gynecologic carcinomas. Nor were any differences from the normal population seen in the frequency of Hp¹ and Hp² genes. A marked increase in PTC tasters was seen in the carcinoma pts. (3.6 times less individuals insensitive to PTC). Higher LDH₅ values were seen in 59.79% of the cancer pts.; and a higher percentage of serum group Gm a+ members was found in these patients.

70-551 HEREDITARY BLOOD AND SERUM TYPES, PTC TEST AND LEVEL OF THE FIFTH FRACTION OF SERUM LACTATEDEHYDROGENASE IN FEMALES WITH GYNECOLOGICAL CANCER. (II. COMMUNICATION). (E.) Miluničová, A. (Charles U., Prague), A. Jandová, L. Laurová, J. Novotná and V. Škoda. Neoplasma (Bratisl.) 16(3):311-316, 1969.

A markedly decreased percentage of PTC non-tasters (compared with normal populations) was observed in 142 women with carcinoma of the uterus, 85 of the cervix, and 50 of the ovary. No difference from the normal population was

seen in 44 women with endometrial atypia. However, an unexplained decrease was seen in 126 women with benign diagnosis. A higher percentage of women with increased LDH₅ level were serum group Gm a+ members in all three carcinoma groups. In pts. with ovarian carcinoma the increase in Gm a+ group members was not dependent on LDH₅ level. A lower frequency of Rh(D) negative and a higher frequency of blood group A was observed in ovarian carcinoma pts. The incidence of Rh(D) negative persons was higher in females with endometrial atypia than in the normal population.

70-552 ATAXIA-TELANGIECTASIA WITH GASTRIC ADENOCARCINOMA. (E.) Haerer, A. F. (2500 N. State St., Jackson, Miss.), J. F. Jackson and C. G. Evers. JAMA 210(10):1884-1887, 1969.

Report of a Negro family in which 5/12 children had ataxiatelangiectasia. Only 2 members were examined closely. Both were female and both died in the second decade of life with adenocarcinoma of the stomach. Decreased IgA levels, decreased lymphoblastic transformation index, chromosomal abnormalities, and abnormal thymic and lymphoid tissues were seen in the one patient studied. The authors conclude that the accepted predisposition to lymphoid neoplasms in ataxia-telangiectasia should be enlarged to include other malignant neoplasms.

70-553 CHANGES IN THE PYRUVATE KINASE AND LACTATE DEHYDROGENASE ACTIVITY IN RAT LUNG DURING CULTIVATION AND "SPONTANEOUS" DEVELOPMENT OF MALIGNANCY IN VITRO. (E.) Guminska, M. (Fibiger Lab., Lyngby, Denmark), P. Briand, J. L. Daehnfelddt and J. Kieler. Europ. J. Cancer 5(6):597-604, 1969.

The pyruvate kinase (PK) activity in Yoshida ascites tumor (YAT) cells was significantly higher than in the lung and liver tissues 2-6-month-old inbred Wistar rats; but the lactate dehydrogenase (LDH) activity differed significantly only from that of lung. The PK and LDH activity of the rat lung tissue increased rapidly during cultivation in vitro and approached the values found in YAT cells. Changes in PK and LDH preceded increased glycolysis and occurred much earlier than in vitro development of malignancy. The authors conclude that high PK and LDH activities could not be used as a criterion of malignant transformation in vitro.

70-554 DEVELOPMENT OF TUMORS, PARTICULARLY MAMMARY TUMORS, IN AGENT-FREE SUBSTRAIN RIIIeB/De MICE. (E.) Deringer, M. K. (NCI, Bethesda, Md.). J. Nat. Cancer Inst. 43(6):1347-1351, 1969.

Mammary tumors developed in 23% of virgin female RIIIe/De mice (produced by transfer of fertilized ova from RIII/AnDe to C57BL/HeDe mice) at av. age of 22.3 mo.; in 41% of the breeding females at av. of 20.1 mo.; and in 40% of the force-bred females at an av. of 19.9 mo. This tumor incidence was lower than that of the RIII/AnDe strain (97% virgin females and 98.5% of the breeding females developed tumors at 11.6 and 7.7 mo., resp.) and the av. tumor age was increased. Reticulum cell neoplasms, lymphocytic neoplasm, lymphosarcoma, fibrosarcomas, pulmonary tumors, hemangioendotheliomas and osteoid tumor of tail were also seen.

70-555 HAMSTER LYMPHOMA, TM. (E.) Banfield, W. G. (NCI, Bethesda, Md.). Nat. Cancer Inst. Monogr. 32:335-336, 1969.

TM reticulum cell sarcoma, derived from a spontaneous tumor in a male Syrian hamster, was transplanted s.c. for 164 passages. No virus was found in association with this tumor, which could be transmitted by cannibalism or by feeding of the tumor cells to non-tumor-bearing animals. The TM tumor usually developed in the larynx and never directly involved the g.i. tract. Transmission of the TM lymphoma was also successful using an insect vector, Aedes aegypti. If the mosquitoes fed on tumor-bearing hosts during the terminal leukemic stage, and if feeding was interrupted and then continued on non-tumor-bearing hamsters, 2% of the mosquitoes transmitted the tumor to the recipients. Transfer of the TM lymphoma by the transfer of cells under all of these conditions (s.c. transplantation, tumor feeding and the insect vector) was confirmed by examination of the tumor cells, which retained the unique male karyotype from the donors to recipients of either sex.

70-556 CHRONIC RUNT DISEASE IN RATS: CLINICAL AND PATHOLOGIC STUDIES. (E.) Abe, T. (Keio U. Sch. Med., Tokyo), S. Shimada and R. Osako. J. Nat. Cancer Inst. 43(2):459-467, 1969.

Mortality from acute runt disease induced in 4-6-week-old (Sprague-Dawley x Wistar) F₁ (SWF₁) rats by i.p. inj. of Wistar spleen cell suspension was reduced by admin. of Metopirone (25 mg p.o./d x 5). No neoplastic changes were observed in long term (more than 12 mo.) survivors.

AUTHOR INDEX

- Aaronson, S. A. 442
 Abe, T. 556
 Adenis, L. 395
 Ajuria, E. 441
 Alcini, E. 390
 Alexandrov, K. 380
 Allen, J. L. 437
 Allison, A. C. 411
 Alquati, P. 390
 Anderer, F. A. 435
 Araki, M. 432
 Azelrod, D. 501

 Ball, J. K. 377
 Balner, H. 391
 Bandy, D. 365
 Banfield, W. G. 555
 Baron, S. 444,461
 Bataillon, G. 466
 Bednarzewski, J. 359
 Belloncik, S. 516
 Bendall, R. 403
 Bender, E. 488
 Bennett, B. 415
 Bentvelzen, P. 481
 Benyesh-Melnick, M. 450
 Beresbi, M. 497
 Bernard, P. 368
 Bertone, C. 519
 Biserter, G. 486
 Biswal, N. 450
 Bloom, B. R. 415
 Bond, H. E. 478
 Bonneau, H. 496,497
 Booth, A. N. 365
 Boulanger, P. A. 486
 Bourali, C. 443
 Bourgaux, P. 494
 Bourgaux-Ramolsy, D. 494
 Bourret, J. 371
 Bradley, R. M. 515
 Brady, R. O. 515
 Brailovsky, C. 516
 Bresson, J.-R. 370
 Briand, P. 553
 Brodey, R. S. 447
 Bryan, G. T. 407,426,427
 Byon, P.-A. 369
 Cardette, W. J. 517
 Carger, M. M. 505
 Carmester, B. R. 511
 Carrows, T. W. 352
 Carstein, N. A. 411
 Carstin, P. 523
 Carter, W. H. 363
 Car-Hoi, N. P. 386

 Chamorro, A. 416
 Champy-Hatem, S. 387
 Chany, C. 462,467
 Charney, J. 474,475
 Chrzanowski, A. 528
 Cikes, M. 446
 Clark, H. F. 471
 Clifford, P. 509,523
 Clouse, J. A. 396
 Codegone, M. L. 418
 Coeur, P. 369
 Cohen, S. M. 426,427
 Cooper, E. H. 536
 Cooper, R. C. 534
 Coppey, J. 443
 Cramer, R. 498
 Cremer, N. E. 439
 Crovetti, A. J. 426
 Crumpacker, C. S. 503
 Curchod, A. 356

 Daams, J. H. 481
 Daehnfelddt, J. L. 553
 Dallenbach, F. 521
 Daniel, M. D. 513
 Dao, T. L. 376
 Dawson, P. J. 436
 de Carvalho, A. R. L. 355
 DeHarven, E. 447
 Demaille, A. 395
 Deringer, M. K. 554
 Der-sjant, H. 391
 de Schryver, A. 523
 de-Thé, G. 523
 Diamond, L. 409
 Diehl, V. 509,523
 Dihmis, C. 543
 DiPaolo, J. A. 385
 Dixon, F. J., Jr. 354
 Dodd, D. C. 469
 Donawick, W. J. 469
 Donovan, P. J. 385
 Doré, J.-F. 441
 Dörken, H. 524
 Driessens, J. 395
 Duchesne, J. 430
 Ducros, M.-C. 476,477,480
 Duesberg, P. H. 465
 Dulbecco, R. 494
 Duplan, J. F. 361
 DuPlessis, L. S. 397

 Ebert, J. S. 455
 Eichel, B. 413
 Ertürk, E. 407,426,427
 Eugster, A. K. 457
 Evers, C. G. 552

 Fahmy, M. J. 382
 Fahmy, O. G. 382
 Falk, H. L. 408

 Faucounau, N. 429
 Fenyö, E. M. 438
 Ferber, K. H. 545
 Ferguson, D. B. 518
 Ferrer, J. F. 445
 Field, A. K. 512
 Fieldsteel, A. H. 436
 Fienberg, R. 548
 Finkelstein, S. 547
 Fischer, P. 546
 Fischinger, P. J. 452,459,460
 Fishbein, L. 410
 Florkiewicz, H. 359
 Fraley, E. E. 506
 Frei, J. V. 402
 Friedman, H. 437
 Friedrich-Frekse, H. 399,400
 Fujinaga, K. 514

 Gallagher, H. S. 538
 Garcia-Giralt, E. 456
 Geering, G. 447
 Gelboin, H. V. 378,381,409
 Gentilhomme, O. 369
 Geraldese, A. 491
 Ghittino, P. 418
 Giau, N.-B. 386,416
 Gibbs, F. A., Jr. 445
 Gignoux, M. 368
 Gilden, R. V. 463
 Gillette, K. G. 470
 Gilmore, C. E. 513
 Girard, R. 369,371,372
 Gliden, R. V. 484
 Glover, E. L. 420
 Goldschmidt, B. M. 419
 Goldstein, D. 495
 Golub, E. 546
 Good, R. A. 431
 Gössner, W. 400
 Graffi, A. 488
 Grantham, P. H. 433,434
 Grasso, P. 351
 Green, M. 514
 Greenawalt, C. 451
 Greenblatt, M. 363
 Grégoire, A. 462,467
 Gresser, I. 443
 Griffiths, K. 412
 Grosdidier, J. 360
 Grözing, K.-H. 521
 Guminska, M. 553
 Gunner, S. W. 403

 Haerer, A. F. 552
 Haguena, F. 454
 Hall, W. T. 468,478
 Hancock, R. 493
 Hanson, L. E. 490
 Hardy, W. D., Jr. 447
 Harse, J. 412

- Hartley, J. W. 440,442,458
 Hata, S. 353
 Hatanaka, M. 463
 Heidelberger, C. 388
 Heisler, H. 521
 Hellman, A. 549
 Hellman, K. B. 549
 Henderson, W. J. 412
 Henle, G. 509,523
 Henle, W. 509,523
 Henry, M. 476,477,480
 Henry, P. H. 503
 Heyden, S. 532
 Hilleman, M. R. 512
 Hirano, S. 437
 Hitchner, S. B. 508
 Hiu, I. J. 456
 Ho, H.-C. 523
 Hoffmann, M. 399
 Hollande, E. 476,477,480
 Holzner, H. 546
 Homburger, F. 384
 Horton, R. E. 433,434
 Huberman, E. 381,401
 Hudson, J. 495
 Huebner, R. J. 408,449,451,
 458,461,463,472,484
 Hunstein, W. 525
 Hunt, R. D. 513
 Hurst, L. 416
- Ichimura, H. 422,428
 Igel, H. J. 408
 Ikegami, T. 425
 Ishimoto, A. 489
 Ito, Y. 489
 Iversen, O. H. 537
 Izard, C. 414
- Jackson, J. F. 552
 Jandová, A. 550,551
 Jaume, F. 486
 Johnstone, C. 469
 Jones, T. C. 513
 Joshi, V. V. 402
- Kachani, Z. F. C. 500
 Kafuko, G. W. 509
 Kallner, G. 530
 Kalter, S. S. 457
 Kantshev, K. 522
 Kasahara, S. 483
 Katz, C. 419
 Kawamura, A., Jr. 483
 Kawazoe, Y. 432
 Keller, C. A. 534
 Kenzy, S. G. 507
 Kern, J. 484
 Kessler, I. I. 541
 Khera, K. S. 403
 Kieff, E. D. 511
- Kieler, J. 553
 Kim, C. S. 457
 Kim, U. 394
 King, N. W. 513
 Kirya, B. G. 509
 Kitamura, I. 518
 Kizer, D. E. 396
 Klein, E. 438
 Klein, G. 509,523
 Klement, V. 440,458
 Kondo, M. 422,428
 Konrad, P. 547
 Koprowski, H. 502
 Kotin, P. 408
 Kovacs, K. 375
 Kratzer, F. H. 365
 Kuhn, W. 488
 Kundel, H. G. 354
 Kunze-Mühl, E. 546
 Kurita, Y. 374
 Kurstak, E. 516
 Kutas, J. 358
- Lacassagne, A. 416
 Laky, R. 358
 Lalich, J. J. 417
 Lampson, G. P. 512
 Lane, W. T. 472
 Lappé, M. A. 389,392
 Laugier, A. 539
 Laurová, L. 550,551
 Lee, D. J. 362
 Lee, L. F. 511
 Legrand, E. 361
 Lemaître, J. 462,467
 Lennette, E. H. 439,448
 Levin, M. J. 503
 Levy, H. B. 378
 Lewis, A. M., Jr. 503
 Lhérisson-Straboni, A. M.
 496
 Lijinsky, W. 363
 Lion, Y. 430
 Log, T. 449
- Macieira-Coelho, A. 456
 Macpherson, I. 485
 Maehara, N. 483
 Maher, V. M. 364
 Makino, S. 483
 Malaise, E. 539
 Mallucci, L. 492
 Malmgren, R. A. 468
 Maraud, R. 429
 Mariage, C. 366,367
 Mark, J. 453
 Marshak, R. R. 469
 Martens, J. G. 469
 Martin, D. H. 549
 Martin, J. E. 469,538
 Martin, M. A. 501
 Martin, P. 370,371
 Mârza, V. D. 540
- Mathé, G. 441
 McAllister, R. M. 484,485
 McDonough, M. 410
 McDonough, S. 447
 McFarland, V. W. 515
 McFarlane, E. S. 487
 McIntire, K. R. 411
 McLean, E. P. 415
 Melchionne, S. 419
 Meléndex, L. V. 513
 Melnick, J. L. 510
 Meneghelli, P. L. 533
 Merz, W. R. 356
 Metcalf, D. 406
 Meyer, G. 496
 Meyer, R. C. 490
 Michelson-Fiske, S. 454
 Mihoc, M. 540
 Miller, J. M. 470
 Miller, L. D. 470
 Miluničová, A. 550,551
 Mizuno, K. 353
 Möbius, G. 526,527
 Mondal, S. 388
 Monjour, L. 366,367
 Montesano, R. 398
 Moore, D. H. 473,474,475
 Moore, M. A. S. 406
 Mora, P. T. 515
 Mori, K. 422,428
 Morris, J. E. 417
 Morrow, R. H. 509
 Morton, D. L. 468
 Moschetto, Y. 486
 Muger, G. M. 405
 Muggler-Bickel, J. 531
 Munube, G. M. R. 509
 Murakami, T. 428
- Nakagawa, M. 483
 Nazerian, K. 511
 Neerhout, R. 547
 Nelson, R. L. 385
 Nemes, M. M. 512
 Neubauer, R. H. 461
 Nicolson, M. O. 484
 Niculescu, M. I. 540
 Nishimura, R. 423
 Nishizuka, Y. 374
 Nordenskjöld, B. A. 438
 Novelli, G. D. 549
 Novotná, J. 550,551
 Nozdryn-Piotnicki, B. 520
 Nunn, J. R. 397
- O'Connor, T. 452
 O'Connor, T. E. 459,460
 Oettgen, H. F. 415
 Ohta, A. 422,428
 Oka, R. 373
 Old, L. J. 415,447
 Olson, C. 470
 Olson, P. R. 404

- Osako, R. 556
 Oshiro, L. S. 439,448
- Palestro, G. 418
 Pandov, H. 379
 Papadopulu, G. 400
 Parietti, R. 360
 Parkes, H. G. 544
 Paulson, D. F. 506
 Pauluzzi, S. 482
 Păvăloiu, I. 540
 Pawlicki, M. 528
 Peckham, M. J. 536
 Pike, P. 509
 Pillsbury, N. 473
 Piña, M. 514
 Pipkin, G. E. 423
 Pister, L. 435
 Póka, L. 358
 Pola, P. 390
 Pollack, R. E. 505
 Ponte, P. L. 519
 Prehn, R. T. 389
 Price, J. M. 417,426,427
 Prince, A. M. 464
 Provana, A. 418
 Pugh, W. E. 440
 Pullinger, B. D. 473,475
- Rabinowitz, Z. 499
 Rabbotti, G. F. 454
 Rabenstein, L. 472
 Raimbert, P. 539
 Rapp, F. 482
 Ratner, I. A. 457
 Rawls, W. E. 510
 Reed, G. 484,485
 Reuber, M. D. 420,424
 Revo, L. 369,372
 Rhim, J. S. 451,472
 Riggs, J. L. 448,485
 Rissberger, A. 507
 Risch, W. A. 397
 Robert, D. 360
 Roizman, B. 511
 Ronzoni, G. 390
 Ronzoni Bernardi, M. G. 533
 Rostrom, C. C. 351
 Rowe, W. P. 440,458
- Rubin, A. B. 500
 Rublińska, B. 520
 Rucleanu, L. 540
 Ruchs, L. 381,401,499
 Ruffiotti, U. 398
- Salvati, A. 519
 Sarkar, N. H. 474
 Sarma, P. S. 449,461
 Sasaki, K. 483
 Schäfer, W. 435
 Schlegel, J. U. 423
 Schlienger, M. 539
 Schneiders, F. 488
 Schramm, T. 488
 Schultz, G. N. 423
 Sekely, L. I. 464
 Semeraro, D. 519
 Shahrik, H. A. 413
 Shanbrom, E. 547
 Sharma, J. M. 507
 Shaw, G. J. 487
 Shimada, S. 556
 Shimkin, M. B. 410
 Shiu, G. 461
 Shubik, P. 421
 Sims, P. 379,383
 Sinnhuber, R. O. 362
 Sivak, A. 419
 Škoda, V. 550,551
 Skolyszewski, J. 528
 Somogyi, A. 375
 Soubrier, B. 370
 Spear, P. G. 511
 Springfield, K. 526,527
 Staszewski, J. 529,542
 Stein, R. J. 417
 Steinberg, A. D. 444
 Stoll, R. 429
 Stoltz, D. R. 403
 Stookey, J. L. 357
 Stutman, O. 393,431
 Sugiyama, T. 374
 Summers, W. C. 364
 Swern, D. 410
- Tachibana, T. 438
 Takada, M. 483
 Takaki, R. 425
 Takemoto, K. K. 504
 Takii, M. 425
 Talal, N. 444
 Tamura, M. 422,428,432
 Taylor, D. O. N. 439,448
 Thomas, J. A. 476,477,479
 480
 Todaro, G. J. 442,504
 Tolot, F. 370,371
 Tomioka, S. 353
 Tompkins, W. A. F. 510
 Tosoni Dalai, M. I. 533
 Toth, B. 421
 Toury, J. 366
- Traut, M. 401
 Treger, A. 384
 Trentin, J. J. 518
 Tubiana, M. 539
 Tukei, P. M. 509
 Turner, H. C. 408,472
 Tytell, A. A. 512
- Uehara, N. 432
 Uhl, N. 525
- Valadaud, D. 414
 Van De Vorst, A. 430
 Van Duuren, B. L. 419
 Van Hoosier, G. L., Jr. 518
 Vendrely, C. 380
 Vendrely, R. 380
 Vernes, A. 395
 Vice, T. E. 457
 Vogt, P. K. 465
 Von Esch, A. M. 426
 Von Niederhäusern, F. 356
 Vorbrodt, A. 502
- Wales, J. H. 362
 Walford, R. L. 547
 Warner, N. L. 406
 Watelet, F. 360
 Watrach, A. M. 490
 Wattenberg, L. W. 404
 Weil, R. 493,495
 Weisburger, E. K. 433,434
 Weisburger, J. H. 433,434
 Wieczorkiewicz, A. 535
 Wieder, R. 410
 Wiese, W. H. 503
 Wiley, M. 365
 Williamson, M. E. 513
 Witkowski, F. 535
- Yang, W.-K. 549
 Yoshikawa-Fukada, M. 455
 Yunis, E. J. 431
- Zayid, I. 543
 Zeigel, R. F. 471
 Ziegler, J. L. 509
 Zschoch, H. 526,527

SUBJECT INDEX

- ACETAMIDE, THIO-
 hepatoma, rat: 400
- ACETYLAMINOFLUORENE (See N-2-Fluorenylacetamide)
- ADRENAL
 dimethylbenzanthracene necrosis, effect of
 spironolactone, rat: 375
- AFLATOXIN(S)
 effect on serum antibodies, mechanism, rat:
 367
 food contamination, review: 366
 liver and kidney tumors, effect of cyclo-
 propenoid fatty acids, rat: 362
 toxicity, chicken: 365
- AFLATOXIN B1
 hepatoma, trout: 418
 liver and kidney tumors, rat: 363
 mutagenesis and effect on DNA, bacteria: 364
- AFLATOXIN B2
 absence of carcinogenic effect, rat: 363
- AFLATOXIN G1
 liver and kidney tumors, rat: 363
- AGE FACTORS
 dimethylbenzanthracene mammary carcinogenesis,
 rat: 376
- AMINO ACIDS
 nucleohistones, adenovirus-12 or SV40/adenovirus-2, hamster tumors: 486
- AMINO ACIDS, AROMATIC
 structure-activity relationships, review: 353
- ANISOLE DERIVATIVES
 skin cancer, mechanism, review: 351
- ANTHRANILIC ACID, 3-HYDROXY- (tryptophan metabolite)
 bladder tumors, effect of ascorbic acid, mouse:
 423
- ANTITUMOR AGENTS
 5-fluorouracil, effect on dimethylbenzanthracene
 skin tumor, mouse: 404
- AROMATIC COMPOUNDS
 structure-activity relationships, review: 353
- ASBESTOS
 identification, mesothelioma, human: 412
- ASCORBIC ACID
 effect on hydroxyanthranilic acid bladder
 tumors, mouse: 423
- AZIRIDINE DERIVATIVES
 lung tumors, bioassay method, mouse: 410
- AZOBENZENE, 4-DIMETHYLAMINO-
 hepatoma, effect of pinealectomy, rat: 416
 + mineral oil, hepatoma, free radical formation,
 rat: 430
- AZOBENZENE, 4'-FLUORO-4-DIMETHYLAMINO-
 hepatoma, nuclear RNA, rat: 396
- AZOBENZENE, 3'-METHYL-4-DIMETHYLAMINO-
 hepatoma
 nuclear RNA, rat: 396
 tumor-specific antigens, rat: 395
- AZOTOLUENE, o-AMINO-
 hepatoma, trout: 418
- 1,2-BENZANTHRACENE
 metabolism, effect of α -naphthoflavone, normal
 cells: 409
- 2-BENZANTHRACENE (benz(a)anthracene)
 transformed cells, benzpyrene cytotoxicity:
 381
- BENZANTHRACENE, 7-BROMOMETHYL-
 metabolism, mouse embryo cell cultures: 383
- BENZANTHRACENE, 7,12-DIMETHYL-
 adrenal necrosis, prevention by spironolactone,
 rat: 375
 cheek pouch tumors, enzymes, hamster: 373
 cytotoxicity and metabolism, effect of α -
 naphthoflavone, normal cells: 409
 leukemia, karyotype, rat: 374
 mammary tumors, age factors, rat: 376
 metabolism, mouse embryo cells: 383
 mutagenesis, *Drosophila*: 382
 skin tumors
 effect of
 antitumor agent, mouse: 404
 synthetic RNA polymer, mouse: 378
 soluble tumor antigens, delayed hypersensitivity
 reaction, guinea pig: 415
 thymic lymphoma, effect of syngeneic bone
 marrow cells, mouse: 377
- BENZANTHRACENE, 7-METHYL-
 metabolism, mouse embryo cells: 383
- BENZENE AND BENZENE DERIVATIVES
 occupational exposure, leukemia: 369,370,
 371,372
- BENZIDINE
 occupational exposure, bladder cancer, U.S.:
 545
- BENZO(rst)PENTAPHENE (See 3,4:9,10-Dibenzpyrene)
- BENZO(a)PYRENE (See 3,4-Benzpyrene)
- BENZO(e)PYRENE
 metabolism, mouse embryo cell cultures: 383
- 3,4-BENZPYRENE (benzo(a)pyrene)
 cytotoxicity
 effect of α -naphthoflavone, normal cells:
 409
 normal or transformed animal or human cells:
 381
 effect on RNA, mouse skin: 380
 metabolism, mouse embryo cells: 383
 reaction with imidazoles, DNA and RNA,
 mechanism: 387
 transformed hamster cells
 cytotoxicity of other carcinogens: 401
 hamster tumors: 385
- BLADDER CARCINOGENESIS
 cyclamates, mouse: 407
 hydroxyanthranilic acid, effect of ascorbic
 acid, mouse: 423
 N-(4-[5-nitro-2-furyl]-2-thiazolyl)formamide,
 rat: 427
- BLADDER NEOPLASMS
 benzidine or β -naphthylamine exposure, U.S.:
 545
 epidemiology
 occupational, Britain: 544
 U.S.: 545
 review: 532
 rubber exposure, Britain: 544
- BLOOD GROUPS
 ABO, Rh and Gm, distribution, female genital
 cancer, Poland: 550,551

- BONE MARROW
transplantation, effect on dimethylbenzanthracene lymphoma, mouse: 377
- BRAIN NEOPLASMS
induction, simian adenovirus (SA7), hamster, properties of cell line: 482
- BREAST NEOPLASMS (See Mammary neoplasms, human)
- BRONCHUS NEOPLASMS
epidemiology
Poland (Gliwice), women: 535
smoking, East Germany: 526
urbanization, East Germany: 527
- CARBAMATE DERIVATIVES
lung tumors, bioassay method, mouse: 410
- CARBOHYDRATES
uptake, mouse sarcoma virus-transformed mouse embryo cells: 463
- CARBON TETRACHLORIDE
hepatoma, rat, strain difference: 420
- CARCINOGENESIS (CHEMICAL)
aromatic compounds, structure-activity relationships, review: 353
mechanism, review: 352
- CELL GROWTH KINETICS
breast cancer: 538
carcinogen-induced skin tumors, mouse: 537
clonal evolution, acute leukemia, human: 540
Hodgkin's disease: 536
lung and lymph node metastases, human: 539
- CERVIX UTERI NEOPLASMS
epidemiology
early lesions, methods: 519
herpesvirus type 2 infection, Texas (Houston): 510
Poland, environmental factors (socioeconomic status, urbanization, occupation): 520
review: 356
- CHOLIC ACID
hamster tumor, viability in vitro at high temperature: 500
- CHROMOSOMES
dimethylbenzanthracene leukemia, rat: 374
effect of cyclamates, human WBC: 403
mineral oil + androgen-induced leukemia, mouse: 406
replication, polyoma virus-infected mouse cells: 493
Rous sarcoma virus-induced mouse sarcomas: 453
spontaneous or radiation-induced leukemia, AKR/T1ALD mouse: 361
- CONNECTIVE TISSUE NEOPLASMS
hemangioendothelial sarcoma, induction, 5-acetamido-3-(5-nitro-2-furyl)-6H-1,2,4-oxadiazine, rat: 426
liposarcoma, cell line, sarcoma virus-like particles, human: 468
multicentric fibromatosis and desmoids, familial: 543
sarcomas, interferon-antagonistic factors, human: 467
spontaneous myxofibroma, C-type virus particles, snake (Vipera russelli): 471
- CORPUS UTERI NEOPLASMS
epidemiology, Poland, environmental factors (occupation, urbanization, socioeconomic status): 520
postmenopausal endometrial cancer, persistent ovarian stromal theca cells: 548
sarcoma, induction, hydroxyaminoquinoline oxide, rat: 428
- CYCLAMATES
bladder tumors, mouse: 407
effect on chromosomes, human WBC: 403
- CYCLOHEXYLAMINE
and derivatives, effect on chromosomes, human WBC: 403
- 1:2,5:6-DIBENZANTHRACENE
skin tumors, accelerated induction method, mouse: 384
- DIBENZ(a,h)ANTHRACENE 5,6-OXIDE
metabolism, rat liver enzyme: 379
- 3,4:9,10-DIBENZOPYRENE (benzo(rst)pentaphene)
skin tumors, accelerated induction method, mouse: 384
- 3,4:9,10-DIBENZOPYRENE, 5-AMINO-
s.c. sarcoma, mouse: 386
- 3,4:9,10-DIBENZOPYRENE, 5-NITRO-
s.c. sarcoma, mouse: 386
- DISEASE TRANSMISSION
cellular, hamster tumor (TM lymphoma), insect vector (Aedes): 555
herpesvirus type 2, venereal, Texas (Houston): 510
mammary tumor virus, effect of host genotype, mouse: 481
Rous sarcoma virus, dexamethasone-treated baboons: 457
- DISTRIBUTION
fluorenylacetamide and derivative, effect of germ-free status, rat: 433,434
nitroquinoline oxide, mouse: 432
- EAR DUCT NEOPLASMS
induction
fluorenylacetamide, rat: 417
5-nitrofur derivatives, rat: 417
- Encephalartos hildebrandtii FLOUR
kidney tumors, rat: 405
- ENDOCRINE ABLATION
effect on fluorenyldiacetamide liver tumors, rat: 424.
pinealectomy, effect on chemical liver carcinogenesis, rat: 416
- ENDOMETRIUM NEOPLASMS (See under Corpus uteri neoplasms)
- ENVIRONMENTAL FACTORS (See also under Foods, Occupational diseases and Water Pollution)
seasons, Hodgkin's disease, Germany (Göttingen): 525
socioeconomic status and occupation, cervix or uterus cancer, Poland: 520
urbanization
bronchus cancer, East Germany: 527
cervix or uterus cancer, Poland: 520

ENVIRONMENTAL FACTORS (contd)

lung cancer, Poland: 529

ENZYMES (See also Isoenzymes)

adenosine triphosphatase, avian myeloblastosis assay method: 464

aryl hydrocarbon hydroxylase, benzpyrene cytotoxicity, normal or transformed cells: 381

dehydrogenases and esterase, hamster cheek pouch or human oral tumors: 373

lactate dehydrogenase

isoenzyme-5 distribution, female genital cancer, Poland: 550,551

rat tumor cells and transforming rat lung cells: 553

muramidase, mineral oil + androgen-induced leukemia, mouse: 406

pyruvate kinase, rat tumor cells and transforming rat lung cells: 553

EPIDEMIOLOGY

all tumors

genetic factors, diabetes mellitus and cancer susceptibility: 541

Israel, methods: 530

Switzerland: 531

bladder cancer

benzidine or β -naphthylamine exposure, U.S.: 545

review: 532

rubber manufacturing, Britain: 544

breast cancer, review: 532

bronchus cancer

Poland (Gliwice), women: 535

smoking, East Germany: 526

urbanization, East Germany: 527

Burkitt lymphoma

review: 355

serum EB virus antibodies, children with tumor (Africa) and normal subjects: 509

carcinoma of gastric stump, malignant transformation risk, Hungary (Pecs) or Poland (Lublin): 358,359

cervix cancer

early lesions, methods: 519

Poland, urban and rural: 520

review: 356

serum herpesvirus type 2 antibodies, Texas (Houston): 510

female genital cancer, genetic factors (serum LDH fractions, blood groups and PTC tasting), Poland: 550,551

g.i. cancer, smoking, Poland: 542

Hodgkin's disease

review: 532

seasonal variations, Germany (Göttingen): 525

worldwide: 524

liver cancer, Bulgaria (southeastern): 522

lung cancer

diabetic or nondiabetic men: 541

Poland, urban and rural: 529

review: 532

melanoma, familial incidence: 533

nasopharynx cancer, serum EB virus antibodies, Hong Kong (Chinese) and East Africa: 523

oropharynx and larynx cancer, Poland (Cracow): 528

EPIDEMIOLOGY (contd)

pancreas cancer, Germany (Heidelberg), chronic pancreatic diseases: 521

serum EB virus antibodies

East Africa, Burkitt lymphoma (children): 509

head/neck tumors: 523

Hong Kong (Chinese), head/neck tumors: 523

normal subjects, Africa and other regions: 509,523

serum herpesvirus type 2 antibodies

venereal transmission, Texas (Houston): 510

stomach cancer, review: 532

uterus cancer, Poland, urban and rural: 520

EPIDEMIOLOGY, VETERINARY

mammary and other tumors, mammary tumor virus-free mouse strain (R111eB/DE): 554

skin papillomas, fish, San Francisco Bay, species specificity and water pollution: 534

EPSTEIN-BARR VIRUS (See under Virus, herpes-type)

ESOPHAGUS NEOPLASMS

epidemiology

review: 532

smoking, Poland: 542

malignant transformation of caustic stenosis: 360

ETHER, BIS(CHLOROMETHYL)-

skin tumors, mouse: 419

ETHERS, HALOGENATED

skin tumors, mouse: 419

FATTY ACIDS, CYCLOPROPENOID

effect on aflatoxin carcinogenesis, liver and kidney, rat: 362

N-2-FLUORENYLACETAMIDE

hepatoma, effect of pinealectomy, rat: 416

mammary and ear duct tumors, rat: 417

metabolism, effect of germ-free status, rat: 434

+ mineral oil, hepatoma, free radical formation, rat: 430

premalignant liver lesions, hormone effects, rat: 424

N-2-FLUORENYLACETAMIDE, N-HYDROXY-

metabolism, effect of germ-free status, rat: 433

FOODS

contamination

dimethylnitrosamine, South Africa (Transkei): 397

mycotoxins, review: 366

Encephalartos hildebrandtii flour, kidney tumors, rat: 405

FORMAMIDE, N-(4-[5-NITRO-2-FURYL]-2-THIAZOLYL)-

bladder tumors, rat: 427

FUNGI

mycotoxins, foods, review: 366

GANGLIOSIDES

analysis, SV40- or spontaneously-transformed tumor-inducing mouse cell lines: 515

GASTROINTESTINAL CARCINOGENESIS

hydroxyaminoquinoline oxide, rat: 428

- GASTROINTESTINAL CARCINOGENESIS (contd)
 5-nitrofurantoin derivatives, rat: 417
- GASTROINTESTINAL NEOPLASMS
 epidemiology, smoking, Poland: 542
- GENETICS, ANIMAL
 autoimmunity, role of DNA and RNA, NZB/NZW mouse: 444
 mammary tumor virus
 agent-free mice (R111B/DE), mammary and other tumor incidence: 554
 hereditary transmission and susceptibility, mouse strains: 481
 Marek's disease virus antigen localization, tumor and host cells, susceptible and resistant chickens: 508
 skin papillomas, fish, species specificity, San Francisco Bay: 534
 strain difference
 carbon tetrachloride hepatoma, rat: 420
 methylcholanthrene immunosuppression and skin carcinogenesis, mouse: 393
- GENETICS, CELLULAR
 effect of chemical carcinogens, mechanism, review: 352
- GENETICS, HUMAN
 diabetes mellitus and cancer susceptibility: 541
 familial
 ataxia-telangiectasia, stomach cancer: 552
 malignant melanoma: 533
 multicentric fibromatosis and desmoids: 543
 HL-A transplantation gene, children with leukemia and their families: 547
 serum LDH fractions, PTC tasting and blood groups, female genital cancer, Poland: 550,551
- GENETICS, MICROBIAL
 mouse sarcoma virus genome, effect on carbohydrate uptake, transformed cells: 463
 polyoma virus, genome transcription pattern, mouse cells: 495
 SV40, gene activity, lytically-infected or transformed mouse cells: 501
- GENITAL NEOPLASMS, FEMALE
 genetic factors (serum LDH fractions, blood groups and PTC tasting), Poland: 550,551
- GLUCOCORTICOID-FREE STATUS
 effect on metabolism of fluorenylacetylacetamide and derivative, rat: 433,434
 urethan-induced lung tumors, mouse: 411
- HEAD AND NECK NEOPLASMS
 epidemiology, serum EB virus antibodies, international (Hong Kong, Africa, France, India): 523
 ethmoid and paranasal sinus tumors, occupational exposure to wood: 368
- HORMONES
 dexamethasone, effect on Rous virus sarcoma induction, baboon: 457
 effect on fluorenyldiacetylacetamide liver tumors, rat: 424
 sensitivity, SV40-induced hamster prostate tumors: 506
- IMMUNITY
 cellular
 feline leukemia virus, lymphomas of cats and other mammals: 447
 group-specific antigen, Rous sarcoma virus-transformed chick embryo or hamster cells: 466
 lymphocyte transformation by tumor extracts, breast cancer: 546
 Marek's disease virus, antigen localization, host genetics, chicken tumors: 508
 simian adenovirus (SA7)-induced hamster brain tumor cell line: 482
 surface antigens, Moloney virus-induced mouse lymphoma cells: 446
 radiation leukemia virus-induced rat lymphoma: 445
 Shope papilloma virus-induced rabbit papilloma cells: 489
 T antigens, abortive polyoma virus infection, mouse cells: 492
 azo dye rat hepatoma: 395
 UV sensitivity of nuclear T and homograft-rejection target areas, polyoma virus-infected cells or hamster tumor: 496
 virus-induced tumors, review: 354
 group-specific antigen, Friend leukemia virus, properties: 435
 HL-A transplantation gene, children with leukemia and their families: 547
 host
 bacterial antigen, effect of Friend leukemia virus, mouse: 437
 delayed hypersensitivity, antigens from carcinogen-induced tumors, guinea pig: 415
 Gross viral leukemia, mouse: 441
 methylcholanthrene-induced mammary tumors, rat: 394
 skin tumors, mouse: 389,392
 Moloney leukemia virus-infected rat: 439
 premalignant diethylnitrosamine liver lesions, rat: 399
 serum antibodies, effect of aflatoxin, mechanism, rat: 367
 thymectomized mouse with transplanted thymoma: 431
 serum EB virus antibodies
 children with Burkitt lymphoma and normal subjects (adults or children), Africa: 509
 head/neck tumors, East Africa and Hong Kong: 523
- IMMUNITY DISORDERS
 autoimmunity, role of DNA and RNA, NZB/NZW mouse: 444
 chronic runt disease, effect of Metopirone, tumor incidence, rat: 556
- IMMUNOSUPPRESSION
 antilymphocyte serum
 effect on methylcholanthrene skin tumors, mouse: 391
 transplantability of bovine lymphoma, calf: 469
 methylcholanthrene, strain difference, mouse: 393

IMMUNOSUPPRESSION (contd)

Metopirone, chronic runt disease, rat: 556

INJURIES (See also under Scar tissue)

caustic esophageal stenosis, malignant transformation: 360

INSECTS

densonucleose virus (DNA-containing), transformation, mouse cells: 516

Drosophila

mutagenesis, dimethylbenzanthracene: 382

SV40 or Rous sarcoma virus: 517

SV40 or Rous sarcoma virus tumors: 517

mosquito (Aedes), vector transmission of hamster tumor (TM lymphoma): 555

INTERFERON

antagonists

isolation, human soft tissue sarcomas: 467

Moloney sarcoma virus-induced T-MSV

hamster tumor: 462

effect on spontaneous leukemia development, AKR mouse: 443

INTESTINE NEOPLASMS

induction, hydroxyaminoquinoline oxide, rat: 428

ISOENZYMES

lactate dehydrogenase, distribution, female genital cancer, Poland: 550,551

ISONICOTINIC ACID HYDRAZIDE

toxicity, hamster: 421

KIDNEY CARCINOGENESIS

aflatoxin

effect of cyclopropenoid fatty acids, rat: 362

sex difference, rat: 363

diethylnitrosamine, mouse leukemia virus

antigen content: 408

Encephalartos hildebrandtii flour, rat: 405

5-nitrofuran derivatives, rat: 417

LACTATION

mammary tumor virus

isolation from milk, mouse: 473,474,475, 477,478

replication sequence, mouse: 477

LARYNX NEOPLASMS

epidemiology, Poland (Cracow): 528

LEUKEMIA, EXPERIMENTAL (See also under Virus, leukemia/lymphoma)

AKR (mouse), spontaneous, effect of interferon: 443

mineral oil + androgen-induced, myelomonocytic, chromosomes and muramidase content, mouse: 406

spontaneous or radiation-induced, karyotype, AKR/T1ALD mouse: 361

LEUKEMIA, HUMAN

acute (myeloblastic or lymphoblastic) cell size variations and clonal evolution: 540

child, HL-A transplantation gene, pts. and their families: 547

LEUKEMOGENESIS, EXPERIMENTAL (See also Radiation leukemogenesis and Virus, leukemia/lymphoma)

dimethylbenzanthracene

chromosomes, rat: 374

LEUKEMOGENESIS, EXPERIMENTAL (contd)

thymic lymphoma, effect of syngeneic bone marrow cells, mouse: 377

dimethylnitrosamine

leukemia virus activation, mouse: 408

thymic lymphoma, pathology, mouse: 402

DNA from human or hamster (papovavirus-induced) tumors, hamster lymphoma: 488

methylcholanthrene, leukemia virus activation, mouse: 408

mineral oil + testosterone, myelomonocytic leukemia, chromosomes and muramidase content, mouse: 406

simian herpesvirus (Herpesvirus saimiri), lymphoma-like disease, owl monkey or marmoset: 513

urethan, leukemia virus activation, mouse: 408

LEUKEMOGENESIS, HUMAN

benzene or toluene derivatives, occupational: 369,370,371,372

LIVER

aflatoxin toxicity, chicken: 365

enzyme, metabolism of phenanthrene or dibenz (a,h)anthracene oxides, rat: 379

free radicals during liver carcinogenesis, rat: 430

LIVER CARCINOGENESIS

aflatoxin

rat: 363

effect of cyclopropenoid fatty acids: 362

trout: 418

aminoazotoluene, trout: 418

azobenzene derivatives, nuclear RNA, rat: 396

carbon tetrachloride, strain difference, rat: 420

diethylnitrosamine

mouse, leukemia virus antigen content: 408

rat: 400

effect of pinealectomy: 416

premalignant lesions, host immunity: 399

dimethylaminoazobenzene

effect of pinealectomy, rat: 416

+ mineral oil, free radical formation, rat: 430

dimethylnitrosamine, trout: 418

fluorenylacetamide

effect of pinealectomy, rat: 416

+ mineral oil, free radical formation, rat: 430

fluorenyldiacetamide, premalignant lesions, hormone effects, rat: 424

methyl dimethylaminoazobenzene, tumor-specific antigens, rat: 395

thioacetamide, rat: 400

LIVER NEOPLASMS

epidemiology, Bulgaria (southeastern): 522

LUNG CARCINOGENESIS

aziridines and carbamates, bioassay method, mouse: 410

diethylnitrosamine, hamster: 398

hydroxyaminoquinoline oxide, rat: 428

urethan, mouse, effect of germ-free status: 411

- LUNG NEOPLASMS
epidemiology
diabetic or nondiabetic men: 541
Poland, urban and rural: 529
review: 532
metastatic, growth rates, human: 539
- LUTEOSKYRINE
food contamination, review: 366
- LYMPHATIC SYSTEM NEOPLASMS
metastatic, growth rates, human: 539
- LYMPHOMA, MALIGNANT, EXPERIMENTAL
bovine lymphosarcoma
nuclear ultrastructure: 470
transplantability, effect of antilymphocyte serum, calf: 469
cat, isolation and properties of syncytium-forming virus: 448
chemically induced, role of leukemia virus, mouse: 408
dimethylbenzanthracene-induced, effect of syngeneic bone marrow cells, mouse: 377
dimethylnitrosamine-induced, pathology, mouse: 402
dog, transmissible venereal tumor, possible viral etiology, review: 357
feline leukemia virus antigens, lymphosarcoma, cats, dogs and other animals: 447
induction
echovirus-12 or reovirus-3 (human), hamster: 518
simian herpesvirus (Herpesvirus saimiri), owl monkey or marmoset: 513
TM reticulum cell sarcoma (hamster), cellular transmission (including insect vectors): 555
- LYMPHOMA, MALIGNANT, HUMAN
Burkitt's
epidemiology, review: 355
serum EB virus antibodies, children, Africa: 509
Hodgkin's disease
cell growth kinetics: 536
epidemiology, review: 532
worldwide: 524
seasonal variations, Germany (Göttingen): 525
lymphosarcoma, feline leukemia virus antigens: 447
tumors other than Burkitt lymphoma, serum EB virus antibodies: 509
- MALIGNANT TRANSFORMATION
caustic stenosis to carcinoma of esophagus: 360
chronic inflammation to cancer of pancreas, Germany (Heidelberg): 521
ulcer resection site to carcinoma of stomach, risk, Hungary or Poland: 358,359
- MAMMARY CARCINOGENESIS, EXPERIMENTAL
5-acetamido-3-(5-nitro-2-furyl)-6H-1,2,4-oxadiazine, rat: 427
dimethylbenzanthracene, rat, age factors: 376
DNA from mouse tumor, virus-positive mammary tumors, mouse: 419
fluorenylacetamide, rat: 417
MAMMARY CARCINOGENESIS, EXPERIMENTAL (contd)
hydroxyaminoquinoline oxide, rat: 428
methylcholanthrene, host immunity, rat: 394
5-nitrofur derivatives, rat: 417
MAMMARY NEOPLASMS, EXPERIMENTAL (See also under Virus, mammary tumor)
incidence, agent-free mouse strain (RilleB/DE): 554
virus structures, mouse: 476
MAMMARY NEOPLASMS, HUMAN
epidemiology, review: 532
growth kinetics: 538
tumor extracts, lymphocyte transformation, normal subjects and breast cancer: 546
- MAREK'S DISEASE
viral antigen localization, host genetics, chicken: 508
MAREK'S DISEASE VIRUS (See under Virus, herpes-type)
- METABOLISM DISORDERS
diabetes mellitus and glucose-6-phosphate dehydrogenase variants, genetic and cancer susceptibility: 541
- 3-METHYLCHOLANTHRENE
immunosuppression, strain difference, mouse: 393
lymphoma, mouse, leukemia virus activation: 408
mammary tumors, host immunity, rat: 394
prostate tumors, rat: 390
s.c. tumors, effect of antilymphocyte serum, mouse: 391
skin tumors
cell growth kinetics, mouse: 537
effect of antilymphocyte serum, mouse: 391
host immunity, mouse: 389,392
strain difference, mouse: 393
soluble tumor antigens, delayed hypersensitivity reaction, guinea pig: 415
transformation, mouse prostate cells: 388
- METOPIRONE
immunosuppression, chronic runt disease, tumor incidence, rat: 556
- MOUTH
intraoral fluid cell metabolism, effect of smoking, human: 413
- MOUTH NEOPLASMS
enzymes, human: 373
epidemiology, Poland (Cracow): 528
- MUTAGENESIS
aflatoxin B₁, bacteria: 364
dimethylbenzanthracene, Drosophila: 382
Rous sarcoma virus or SV40, Drosophila: 517
- MYCOTOXINS (See under Fungi)
- α-NAPHTHOLAVONE
effect on cytotoxicity and metabolism of carcinogens, normal cells: 409
- β-NAPHTHYLAMINE
occupational exposure, bladder cancer, U.S.: 545
- NASOPHARYNX NEOPLASMS
serum EB virus antibodies, Hong Kong (Chinese) and East Africa: 523

NEOPLASMS, EXPERIMENTAL

- benzpyrene-transformed cells, hamster sarcoma: 385
- fibrosarcoma, dexamethasone-treated, Rous sarcoma virus-exposed baboon: 457
- thymus cell cultures transformed by nitroso-guanidine derivative, rat: 425
- incidence, mammary tumor virus-free mouse strain (RilleB/DE): 554
- Krebs-2 carcinoma (mouse), DNA from, induction of virus-containing mammary tumors, mouse: 419
- L-M cell-induced (mouse), isoaccepting transfer RNA structure: 549
- sarcoma, induction, human echoviruses or respiratory syncytial virus, hamster: 518
- spontaneously-transformed cells
- ganglioside analysis, mouse: 515
- rat lung, pyruvate kinase and lactate dehydrogenase: 553
- SV40-transformed mouse cells, ganglioside analysis: 515
- Yoshida sarcoma (rat), pyruvate kinase and lactate dehydrogenase: 553

NEOPLASMS, HUMAN

- all tumors
- epidemiology, Israel, methods: 530
- Switzerland: 531
- DNA from, lymphoma induction, hamster: 488
- mesothelioma, identification of asbestos fibers: 412

5-NITROFURAN DERIVATIVES

- mammary, kidney, g.i. or ear duct tumors, rat: 417

NITROSAMINE, DIETHYL-

- hepatoma, rat: 400
- effect of pinealectomy: 416
- liver or lung tumors, leukemia virus antigen content, mouse: 408
- lymphoma, leukemia virus activation, mouse: 408
- premalignant liver lesions, host immunity, rat: 399
- upper respiratory tumors, hamster: 398

NITROSAMINE, DIMETHYL-

- cytotoxicity, normal or transformed hamster or human cells: 401
- food contamination, South Africa (Transkei): 397
- hepatoma, trout: 418
- transformed hamster cells
- cytotoxicity of nitrosomethylurea or dimethylnitrosamine: 401
- reproduction and viability at high temperature: 500

N-NITROSOGUANIDINE, N-METHYL-N'-NITRO-

- transformation, rat thymus cell cultures: 424

4-NITROQUINALDINE-N-OXIDE

- cytotoxicity, effect of adaptation to tobacco smoke, marine plankton: 414

4-NITROQUINOLINE

- s.c. sarcoma, mouse: 422

4-NITROQUINOLINE 1-OXIDE

- cytotoxicity, effect of adaptation to tobacco smoke, marine plankton: 414
- metabolism and distribution, mouse: 432

N-NITROSOUREA, N-METHYL-

- cytotoxicity, normal or transformed hamster and human cells: 401
- thymic lymphoma, pathology, mouse: 402

NUCLEIC ACIDS, DNA

- avian tumor virus-infected chick embryo cells: 465
- cellular (mammalian, plant, bacterial, yeast) or viral, hybridization, Rous sarcoma virus RNA: 455
- effect of aflatoxin
- bacteria: 364
- serum antibody formation, rat: 367
- from human or hamster (papovavirus-induced) tumors, lymphoma induction, hamster: 488
- from mouse carcinoma, induction of virus-containing mammary tumors: 419
- human adenoviruses, group-specificity: 514
- Marek's disease virus, comparison to cyto-megalovirus DNA: 511
- polyoma virus-infected mouse cells: 492,493
- reaction with benzpyrene, mechanism: 387
- ring-type, polyoma virus, replication pattern, mouse embryo cells: 494
- Rous sarcoma virus stimulation, mechanism, human cells: 456
- SV40-infected or transformed cells: 501

NUCLEIC ACIDS, RNA

- human adenovirus-infected cells, group-specificity: 514
- effect of carcinogen, mouse skin: 380
- isoaccepting transfer RNA, structure, L-M cell cultures and L-M cell-induced mouse tumors: 549
- Moloney sarcoma-leukemia virus complex, properties, transformed cells: 450
- nuclear, azobenzene derivative hepatoma, rat: 396
- polyoma virus
- genome transcription pattern, mouse cells: 495
- infected cells: 495
- reaction with benzpyrene, mechanism: 387
- Rous sarcoma virus
- hybridization, DNA of viral or cellular (mammalian, plant, bacterial, yeast) origin: 455
- infected chick embryo cells: 454
- SV40-infected or transformed cells: 501

NUCLEIC ACIDS, RNA, SYNTHETIC POLYMER

- (polyinosinic-polycytidylic acid)
- autoimmunity induction, NZB/NZW mouse: 444
- effect on

- dimethylbenzanthracene skin tumors, mouse: 378
- mouse leukemia or sarcoma virus in vitro: 451

- Rous sarcoma or Marek's disease virus infection, chicks: 512
- virus-induced sarcoma, mouse: 461

NUCLEOHISTONES

- properties, adenovirus-12 or adenovirus-2/SV40 hamster tumors: 486

OCCUPATIONAL DISEASES

- benzene or toluene derivatives, leukemia: 369,370,371,372

OCCUPATIONAL DISEASES (contd)

- bladder cancer
 - β-naphthylamine or benzidine exposure, U.S.: 545
 - rubber manufacturing, Britain: 544
 - occupational status, cervix or uterus cancer, Poland: 520
 - wood exposure, ethmoid and paranasal sinus tumors: 368
- ## OIL, MINERAL
- + dimethylaminoazobenzene or fluorenylacetamide, hepatoma, free radical formation, rat: 430
 - transplantable myelomonocytic leukemia, chromosomes and muramidase content, mouse: 406

- ## OVARY
- persistent stromal theca cells, postmenopausal women with endometrial cancer: 548
- ## 6H-1,2,4-OXADIAZINE, 5-ACETAMIDO-3-(5-NITRO-2-FURYL)-
- hemangioendothelial sarcoma, and mammary tumors, rat: 426

PANCREAS NEOPLASMS

- epidemiology, Germany (Heidelberg), chronic pancreatic diseases: 521

PHARYNX NEOPLASMS

- epidemiology, Poland (Cracow): 528

PHENANTHRENE 9,10-OXIDE

- metabolism, rat liver enzyme: 379

POLYINOSINIC-POLYCYTIDYLIC ACID (See Nucleic acids, RNA, synthetic polymer)

PROSTATE

- cell line, methylcholanthrene transformation, mouse: 388

PROSTATE NEOPLASMS

- induction
 - methylcholanthrene, rat: 390
 - SV40, hormone sensitivity, hamster: 506

ROTEIN SYNTHESIS

- Rous sarcoma virus-infected chick embryo cells: 454

QUINOLINE, 4-HYDROXYAMINO-, 1-OXIDE HCl

- stomach and other tumors, rat: 428

RADIATION EFFECTS

- transformed hamster embryo cells, reproduction and viability at high temperature: 500
- UV sensitivity of polyoma virus target areas: 496

RADIATION LEUKEMOGENESIS

- mouse, karyotype: 361

RADIOACTIVE ISOTOPES AND ELEMENTS

- ¹³¹I, with propylthiouracil, thyroid tumors, rat: 429

RESPIRATORY CARCINOGENESIS

- diethylnitrosamine, upper respiratory tract, hamster: 398

RIB

- occupational exposure, bladder cancer, Britain: 544

SCAR TISSUE (See also under Injuries)

- caustic esophageal stenosis, malignant transformation: 360
- fibromatosis and desmoids, familial: 543
- gastrectomy stump, risk of malignant transformation, Hungary or Poland: 358,359

SEX DIFFERENCE

- aflatoxin kidney tumors, rat: 363

SKIN

- RNA, effect of benzpyrene, mouse: 380

SKIN CARCINOGENESIS

- anisoles, mechanism, review: 351
- bis(chloromethyl)ether, mouse: 419
- dibenzanthracene or dibenzpyrene, accelerated induction method, mouse: 384
- dimethylbenzanthracene
 - cheek pouch, enzymes, hamster: 373
 - effect of synthetic RNA polymer, mouse: 378
- halogenated ethers, mouse: 419
- methylcholanthrene (mouse)
 - cell growth kinetics: 537
 - effect of antilymphocyte serum: 391
 - host immunity: 389,392
 - strain difference: 393

S.C. SARCOMA

- amino- or nitrodibenzpyrene, mouse: 386
- 4-nitroquinoline, mouse: 422

SKIN NEOPLASMS

- fish (papillomas), San Francisco Bay, species specificity and water pollution: 534
- melanoma, familial: 533

SPIRONOLACTONE

- effect on dimethylbenzanthracene adrenal necrosis, rat: 375

STOMACH

- ulcer, cancer of gastrectomy stump, Poland or Hungary: 358,359

STOMACH NEOPLASMS

- ataxia-telangiectasia, familial: 552
- epidemiology
 - review: 532
 - smoking, Poland: 542
- gastric stump, risk, Hungary or Poland: 358, 359
- induction, hydroxyaminoquinoline oxide, rat: 428

SV40 (See under Virus, papova)

TEMPERATURE

- high, reproduction and viability of transformed cells: 500

TESTOSTERONE

- myelomonocytic leukemia, chromosomes and muramidase content, mouse: 406

THYMUS

- cell cultures, transformation, nitrosoguanidine derivative, rat: 424

THYMUS NEOPLASMS

- induction, hydroxyaminoquinoline oxide, rat: 428
- transplantable, functioning as normal thymus, mouse: 431

- THYROID NEOPLASMS
induction, propylthiouracil and ¹³¹I, rat:
429
- TOBACCO SMOKE
adaptation, effect on nitroquinoline oxide or
nitroquinaldine oxide cytotoxicity, marine
plankton: 414
- TOBACCO SMOKING
bronchial cancer, East Germany: 526
effect on oral fluid cells, human: 413
g.i. cancer, Poland: 542
- TOLUENE DERIVATIVES
occupational exposure, leukemia: 372
- TOXICITY
aflatoxin mixture, chicken: 365
isonicotinic acid hydrazide, hamster: 421
- TRAUMA (See Injuries)
- TRYPTOPHAN METABOLITES
bladder tumors, effect of ascorbic acid, mouse:
423
- URACIL, PROPYLTHIO-
with ¹³¹I, thyroid tumors, rat: 429
- URBANIZATION (See under Environmental factors)
- URETHAN
lung tumors, mouse: 410
effect of germ-free status: 411
lymphoma, leukemia virus activation, mouse:
408
- UTERUS NEOPLASMS (See Corpus uteri neoplasms)
- VASCULAR NEOPLASMS
hemangioendothelial sarcoma, induction, 5-
acetamido-3-(5-nitro-2-furyl)-6H-1,2,4-
oxadiazine, rat: 426
- VIRAL CARCINOGENESIS
cellular antigens, review: 354
echovirus-12, -22, -23 and -29 (human),
hamster: 518
reovirus type 3 (human), hamster: 518
respiratory syncytial virus (human), hamster:
518
- VIRUS
human
paramyxovirus, hamster screening: 518
picornavirus, hamster screening: 518
insect, denonucleose (DNA virus), transforma-
tion, mouse cells: 516
- VIRUS, ADENO-
human
DNA-RNA hybridization: 455,514
Group C, virus-specific RNA, transformed
rat cells: 514
Group D, properties: 484
- SA7 (simian)
hamster brain tumor cell line, properties:
482
transformation, hamster or rat cells and
hamster tumors: 485
type 2 (human)/SV40 hybrid
hamster tumor, nucleohistone analysis: 486
nondefective strain (Ad.2+ND₁), properties:
503
type 12 (human)
DNA hybridization with Rous sarcoma virus
RNA: 455
- VIRUS, ADENO- (contd)
hamster tumors
cell line, properties: 483
nucleohistones, analysis: 486
transformed gerbil cells, properties: 487
type 19 (human)
transformed hamster cells, hamster tumor
induction: 484
type 26 (human)
transformed hamster cells, hamster tumor
induction: 484
- VIRUS, HERPES
Group B cytomegaloviruses, comparison to
Marek's disease virus: 511
human, herpes simplex, hamster screening: 518
simian (Herpesvirus saimiri), lymphoma induc-
tion, owl monkey or marmoset: 513
type 2
distribution, Texas (Houston), venereal
transmission: 510
serum antibodies, cervix cancer: 510
- VIRUS, HERPES-TYPE
Epstein-Barr (human)
serum antibodies, African children with
Burkitt lymphoma: 509
nasopharynx cancer, East Africa and
Hong Kong: 523
normal subjects, Africa and other
regions: 509,523
Marek's disease (chicken)
comparison to cytomegaloviruses (group B):
511
infection, effect of synthetic RNA polymer
(polyinosinic-polycytidylic acid),
chick: 512
JM isolate (with/without A- or B-subgroup
resistance-inducing factor virus),
viral antigen localization, host
genetics, chicken: 508
WSU-GF isolate, properties, chicken kidney
cultures: 507
- VIRUS, HYBRID
adenovirus-2/SV40
hamster tumors, nucleohistones, isolation
and properties: 486
nondefective strain (AD.2+ND₁), properties:
503
- VIRUS, LEUKEMIA/LYMPHOMA
AKR (mouse)
infection, effect of interferon, AKR mouse:
443
avian leukosis, particles resembling,
spontaneous connective tissue tumor of
snake (Vipera russelli): 471
avian myeloblastosis-associated, subgroup B
(MAV-2), cellular DNA synthesis, pre-
infected chick embryo cells: 465
BAI strain A avian myeloblastosis, assay
method, in vitro and chicken plasma: 464
dog, transmissible venereal tumor, review:
357
feline leukemia virus
antigen distribution, lymphosarcomas and
other diseases, cats and other mammals:
447
complex with Moloney sarcoma virus, human
leukemia virus indicator: 460

VIRUS, LEUKEMIA/LYMPHOMA (contd)

- trans-specific infectivity: 459,460
- trans-specific rescue of defective mouse sarcoma virus, hamster tumor cells: 449
- feline syncytium-forming agent, isolation and properties: 448
- Friend (mouse)
 - effect of synthetic RNA polymer, Moloney sarcoma or M-MSV(FL) pseudotype virus-infected cells: 451
 - group-specific antigen, properties: 435
 - infection, effect of lymphatic leukemia virus, mouse: 436
 - host immunity to bacteria, mouse: 437
- Friend-associated lymphatic leukemia virus (mouse)
 - effect on Friend leukemia virus splenomegaly, mouse: 436
- genetic susceptibility, mechanism, NZB/NZW mouse: 444
- Gross (mouse)
 - group-specific antigen, properties: 435
 - host immunity, mouse: 441
- human
 - possible indicator, Moloney sarcoma virus/feline leukemia virus complex: 460
- Moloney (mouse)
 - assay, mouse bone marrow cell line: 438
 - cell surface antigens, mouse lymphoma cultures: 446
 - host immunity, rat: 439
 - Moloney sarcoma virus complex, properties of RNA, transformed cells: 450
- Moloney M-MSV(FL) pseudotype (mouse)
 - effect of synthetic RNA polymer, Friend leukemia virus-infected cells: 451
- mouse
 - assay, method, mixed mouse embryo-Rous sarcoma virus-transformed rat cell cultures: 440
 - isolation, tumorigenic mouse embryo cell line: 442
 - possible activation by chemical carcinogens: 408
- radiation leukemia virus (RadLV)
 - loss of virus particles and specific surface antigen, rat: 445
- rat
 - assay, method, mixed rat (Rous sarcoma virus-transformed) and mouse (embryonic) cell cultures: 440
- Rauscher (mouse)
 - group-specific antigen, properties: 435
- type C particles
 - mouse mammary tumor: 476

IS, MAMMARY TUMOR

- mouse
 - agent-free strain (R111eB/DE), incidence of mammary and other tumors: 554
 - hereditary transmission, effect of host genotype: 481
 - high-yield isolation method, C3H mouse milk: 478
 - isolation and titration, R111 mouse milk: 473,474,475
 - replication sequence during lactation: 477

VIRUS, MAMMARY TUMOR (contd)

- structure: 480
- Type A and B particles, mouse mammary tumor: 476
- virus-containing tumors induced by Krebs-2 carcinoma cell DNA: 419
- VIRUS, PAPOVA (papilloma-polyoma-vacuolating)
 - bovine papilloma
 - transformation, hamster embryo cells: 491
 - canine oral papilloma virus
 - structure: 490
 - hamster papovavirus
 - DNA, lymphoma-inducing effects, hamster: 488
 - polyoma
 - abortively infected cells, DNA and T antigen: 492
 - hamster tumors
 - pathology: 497
 - viability at high temperature: 500
 - induction of chromosome replication, mouse cells: 493
 - replication of ring-shaped DNA, mouse embryo cells: 494
 - specific inhibitor, infected hamster cells: 498
 - transformed cells
 - carcinogen cytotoxicity: 401
 - reversion: 499
 - viability and reproduction at high temperature: 500
 - UV sensitivity of target areas: 496
 - viral genome transcription, mouse cells: 495
 - Shope papilloma (rabbit)
 - specific surface antigen, papilloma cells: 489
- SV40
 - adenovirus-2 hybrid
 - hamster tumor, nucleohistone analysis: 486
 - nondefective strain (AD.2⁺ND₁), properties: 503
 - DNA, hybridization (Rous sarcoma virus RNA): 455
 - gene activity, lytic infection, monkey kidney cells: 501
 - hamster tumor, viability at high temperature: 500
 - mutagenesis and tumor induction, Drosophila: 517
 - rescued mutant strains, properties: 504
 - transformed cells
 - hamster prostate, hormone sensitivity of prostate tumors: 506
 - human, cytotoxicity of benzpyrene or dimethylnitrosamine: 401
 - mouse, viral gene activity: 501
 - reproduction and viability at high temperature: 500
 - surface properties: 502,505
 - tumorigenic mouse cell lines, ganglioside types: 515
- VIRUS, SARCOMA
 - FBJ osteosarcoma (mouse)
 - transformation, rat embryo cells: 472

VIRUS, SARCOMA (contd)

- Friend M-MSV(FLV) pseudotype (mouse)
 - tumor development, effect of synthetic RNA polymer, mouse: 461
- Gross pseudotype (mouse)
 - transformed mouse embryo cells, carbohydrate uptake: 463
- Harvey (mouse)
 - defective, rescue by feline leukemia virus, hamster tumor cells: 449
 - transformed cells, carbohydrate uptake, mouse embryo cells: 463
- Kirsten (mouse)
 - hamster tumor, hamster-specific, focus-forming and sarcoma-inducing virus: 458
 - rescue by feline leukemia virus, hamster tumor cells: 449
- Moloney (mouse)
 - competent and defective, properties: 452
 - defective
 - feline leukemia virus complex, trans-specific infectivity: 459,460
 - rescue by feline leukemia virus, hamster tumor cells: 449
 - effect of synthetic RNA polymer, Friend leukemia virus-infected cells: 451
 - hamster tumor (T-MSV), interferon-antagonistic factors: 462
 - M-MSV(MLV) pseudotype, effect of synthetic RNA polymer on tumor development, mouse: 461
 - Moloney leukemia virus complex, properties of RNA, transformed cells: 450
- particles resembling, human liposarcoma cell line: 468
- Rauscher pseudotype (mouse)
 - transformed mouse embryo cells, carbohydrate uptake: 463
- Rous-associated
 - subgroups A (RAV-1) C (RAV-7) or C (RAV-50), cellular DNA synthesis, preinfected

VIRUS, SARCOMA (contd)

- chick embryo cells: 465
- Rous (chicken)
 - #559 strain, mutagenesis and tumor induction, Drosophila: 517
- Bryan strain
 - cellular DNA synthesis, preinfected chick embryo cells: 465
 - RNA, hybridization, DNA of viral and cellular (mammalian, plant, bacterial or yeast) origin: 455
 - tumor induction and mutagenesis, Drosophila: 517
- DNA synthesis stimulation, mechanism, human cells: 456
- exposure, tumor development, dexamethasone-treated baboon: 457
- hamster tumors, group-specific antigen for avian leukosis-sarcoma virus complex: 466
- infection, effect of synthetic RNA polymer (polyinosinic-polycytidylic acid), chick: 512
- Schmidt-Ruppin strain
 - mouse tumors, chromosomes: 453
 - mutagenesis and tumor induction, Drosophila: 517
 - RNA and protein synthesis, chick embryo cells: 454
- transformed cells
 - rat, mixed-culture bioassay for leukemia viruses: 440
 - chick embryo or hamster, group-specific antigens: 466

WATER POLLUTION

- skin papillomas, fish, San Francisco Bay: 534

WOOD

- occupational exposure, ethmoid sinus tumors: 367

U.S. DEPARTMENT OF
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APRIL-MAY 1970

Abstract Nos. 557-989

Vol. 8

No. 4-5

CARCINOGENESIS ABSTRACTS

National Cancer Institute

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE • National Institutes of Health

CARCINOGENESIS ABSTRACTS

Volume 8, Numbers 4-5
April - May 1970

Abstract Numbers
557-989

CONTENTS

	<u>Page</u>
Review	117
Physical Carcinogenesis	121
Chemical Carcinogenesis	123
Viral Carcinogenesis	153
Epidemiology and Biometry	177
Miscellaneous	191
Author Index	i
Subject Index	vi

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Prepared by Scientific Literature Corporation
Philadelphia, Pennsylvania 19103

S. Sim Kessler, Director

Editorial Advisors: Leila Diamond, Ph.D.
Wistar Institute, Philadelphia

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Persuant to a Contract with the Public Health Service
U.S. Department of Health, Education and Welfare
PH43-70-2036

Use of funds for printing this publication approved
by the Director of the Bureau of the Budget on July 25, 1967.

FOREWORD

The National Cancer Institute, in response to Congressional interest and desire for a national program of cooperative research in cancer, is establishing a means whereby information in the field of carcinogenesis will be coordinated and made available. The information to be included will be obtained from the National Cancer Institute, other governmental agencies, and non-governmental research institutions.

The issuing of Carcinogenesis Abstracts under the auspices of the National Cancer Institute will provide a central source for current abstracting of the carcinogenesis literature being published throughout the world. This will help facilitate an integrated and cooperative program of investigation in this area. The growing number of publications in the area of carcinogenesis makes imperative the availability of an appropriate abstracting service so that investigators may be apprised of progress with a minimum of delay. It is our desire to provide the investigator with a readily systematized compilation of the published work.

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NOTE

Journal names are abbreviated according to the list of abbreviations used by Index Medicus. If the journal is not covered by Index Medicus, then the abbreviations (with some modifications) found in World Medical Periodicals, 3rd Edition, are used.

ABBREVIATIONS USED IN ABSTRACTS

admin.	administered, administration	mg	milligram(s)
av.	average	min.	minute(s)
C	curie(s)	ml	milliliter(s)
mC	millicurie(s)	mm	millimeter(s)
uC	microcurie(s)	mo.	month(s)
cm	centimeter(s)	MTD	maximum tolerated dose
conc.	concentration	NIH	National Institutes of Health, USA
cpm	counts per minute	p.o.	orally
DNA	deoxyribonucleic acid	QO ₂	oxygen quotient
DNase	deoxyribonuclease	PFU	plaque forming unit
e.g.	for example	ppm	parts per million
FU	focus forming unit	pt.(s)	patient(s)
i.	gastrointestinal	RBC	red blood cells (erythrocytes)
g	gram(s)	RES	reticuloendothelial system
b	microgram(s)	resp.	respectively
a.	hemoglobin	RNA	ribonucleic acid
D50	intra-arterial	RNase	ribonuclease
nj.	median infectious dose	soln.	solution
noc.	injected, injection(s)	s.c..	subcutaneous
p.	inoculated, inoculation(s)	TCID	tissue culture infectious dose
U.	intraperitoneal	x	times (e.g. x 3/wk.)
v.	international unit(s)	U	unit
50	intravenous	UV	ultraviolet
	kilogram(s)	vol.	volume
	median lethal dose	VA	Veterans Administration
	molar, mole(s)	wt.	weight
	millimole(s)	WBC	white blood cells (leukocytes) or white blood cell count
x.	micromole(s)	yr.	year(s)
	maximum		

LANGUAGE ABBREVIATIONS

Afrikaans	E.	English	Hun.	Hungarian	Lith.	Lithuanian	Ser.	Serbo-Croatian
Arabic	Eston.	Estonian	lc.	Icelandic	Maced.	Macedonian	Sl.	Slovene
Bulgarian	Fin.	Finnish	In.	Indonesian	Nor.	Norwegian	Sp.	Spanish
Chinese	Fr.	French	It.	Italian	Pol.	Polish	Sw.	Swedish
Czech	Ger.	German	Jap.	Japanese	Por.	Portuguese	Th.	Thai
Danish	Gr.	Greek	Kor.	Korean	Rum.	Rumanian	Uk.	Ukrainian
Dutch	Heb.	Hebrew	Latv.	Latvian	Rus.	Russian	Viet.	Vietnamese

70-557 Are the Pills Safe? Barber, H. R. K., E. A. Graber and J. J. O'Rourke. Charles C. Thomas, Springfield, Ill., 1969, 103 pp., \$6.75. (693 references)

Chapter 4 (pp. 24-31) is a discussion of the potential carcinogenic effects of estrogen-progestagen contraceptives. It is concluded that although short-term follow-up studies have demonstrated no apparent increase in carcinogenic potential, long-term studies of large pt. groups (including large control groups) are required to determine the carcinogenic effects (if any) of these contraceptives on the cervix, endometrium and breast.

70-558 The Nature of Melanoma. McGovern, V. J. and M. M. L. Brown. Charles C. Thomas, Springfield, Ill., 1969, 184 pp., \$12.75. (421 references)

Chapter 6 of this book (pp. 60-91), a discussion of nevi, includes brief references to the possibilities of malignant transformation of cutaneous nevi. Chapter 7 (pp. 92-116) and Chapter 8 (pp. 117-126) include extensive discussions of the role of solar exposure in fair-skinned persons predisposed to sunburn and freckling rather than tanning, with particular reference to epidemiologic data obtained from Australia.

70-559 GENE-SELECTION THEORY OF CANCER CAUSATION. (E.) Stewart, A. (U. Oxford, England). Lancet 1(7653):923-924, 1970. (16 references)

The gene-selection theory, stating that non-specific cell injury is the basic cause of cancers, links these diseases with benign tumors, with tissue repair mechanisms and with normal growth and development. In stating that dormant genes are the means by which individuals are protected from radiation damage, this theory also links this mechanism with one that gives to each generation an opportunity to retrieve mistakes of previous generations (hereditary mechanism), and to each species a chance to cope with a hostile environment (evolutionary mechanism). Thus, the gene-selection theory provides a comprehensive theory of cancer etiology and also places malignant diseases in a new perspective.

0-560 THE BLASTOID TRANSFORMATION OF THE LYMPHOCYTES AND ITS SIGNIFICANCE. (E.) Simu, G. (Oncol. Inst., Cluj, Rumania) and . Olinici. Rev. Roumaine Emb. Cytol. 5(2): 03-114, 1968. (109 references)

he general nature of blastoid transformation of lymphocytes and the biological significance of

this phenomenon are discussed. Modification of blastogenesis in leukemias, malignant lymphoma, pts. with cancer and other pathological states is mentioned.

70-561 A REVIEW ON HUMAN LEUKEMIAS FOLLOWING RADIOTHERAPY IN JAPAN. (E.) Kitabatake, T. (Niigata U. Sch. Med., Japan) and S. Kurokawa. Acta Med. Biol. (Niigata) 17(1):1-8, 1969. (23 references)

Data are presented for 49/52 pts. who developed leukemia following radiotherapy (RT) for other diseases, as reported in the Japanese literature through 1966. The relative frequencies of the diseases treated by RT in this pt. group, and the types of leukemia developing in these pts., were about the same as in all of Japan. No evidence was found to support the hypothesis that acute myeloid leukemia is more frequent after exposure to RT than in other radiation-exposed persons. These pts. showed a significantly above-expected number of cases in the 30-60 yr. age range. Latent periods for these RT-induced leukemias, as for radiation-induced cancers other than leukemia, followed a nearly log-normal distribution curve. No correlation was seen between the latent period and the age at RT. The relationship between RT dosage and the latent period was not clear, although high RT doses showed a slight tendency to be associated with short latent periods.

70-562 JOHN HUNTER AND AFTER: RENAL CALCULI AND CANCER OF THE BLADDER. (E.) Pyrah, L. N. (U. Leeds, England). Ann. Roy. Coll. Surg. Eng. 45(1):1-22, 1969. (43 references)

Recent and past work on cancer of the bladder is reviewed with respect to chemical carcinogens (1-naphthylamine; 2-naphthylamine and its metabolites, 2-amino-1-naphthol and 2-naphthylhydroxylamine, benzidine, auramine and magenta, 4-amino-diphenyl; also bracken fern, tobacco and tryptophan) and the response of the transitional epithelium to these stimuli.

70-563 PATHOGENESIS OF TUMORS: HORMONAL AND TISSUE INFLUENCES ON TUMORS. I. (It.) Zironi, A. (U. Milan, Italy). Minerva Med. 60(11):433-438, 1969. (7 references)

The author concludes that all tissues produce substances which stimulate or retard proliferation of their own cells; that cancer cells are more sensitive than other cells to stimulating hormones and less sensitive to retarding hormones, although retaining the type of sensitivity corresponding to the cells from which they were derived; and that the process by which all tissues tend to eliminate aging or damaged cells

("cytocatheresis") is fully in agreement with Baserga's concept of homeocytostasis.

- 70-564 PATHOGENESIS OF TUMORS: CYTOCATHERESIS AND ENHANCEMENT. II. (It.) Zironi, A. (U. Milan, Italy). Minerva Med. 60(11):439-442, 1969. (17 references)

Tissue life is controlled by a "cytocatheretic" hormone, whose presence in surrounding, normal tissue or in grafts of normal or neoplastic tissue, has the power to normalize tumor tissue gradually. Tumor tissue, in turn, contains a thus-far unidentified substance which is not present in normal tissue and which acts to enhance or retard tumor growth and/or acceptance of a tumor graft by increasing or decreasing responsiveness to the cytocatheretic hormone, depending on the frequency and size of dosage when it is extracted and readministered to experimental subjects.

- 70-565 THE POLYADENOMATOSES. (Fr.) Paupe, J. (Hosp. Sick Child., Paris) and J. Saint-Martin. Gaz. Med. Fr. 76(11):2225-2230, 1969. (15 references)

A discussion of the diagnosis, pathogenesis and treatment of simultaneously occurring adenomas of the pituitary, pancreas and parathyroid (sometimes in association with adenomas of the thyroid and adrenals and/or with recurrent peptic ulcer) concludes that recent familial studies suggest an hereditary disorder transmitted by an autosomal dominant gene with virtually total penetration, expressing itself in individual cases by the occurrence of peptic ulcer alone, Zollinger-Ellison syndrome, or multiple endocrine adenomatosis with or without concurrent peptic ulcer.

- 70-566 IMMUNOLOGIC PROBLEMS IN CANCER RESEARCH. (Ger.) Sorkin, E. (Swiss Res. Inst., Davos Platz). Praxis 58(24):765-770, 1969.

The immunologic bases of tumor growth and tumor rejection are discussed. Indications for the existence of tumor-specific antigens in virus and carcinogen-induced tumors and the existence of immunologic defense and control mechanisms are presented. It was shown that immunologic tolerance, the "enhancement" phenomenon (tumor cell-protecting antibodies) and immunosuppression caused by carcinogens, viruses, irradiation or therapeutic drugs are responsible for the failure of immunologic surveillance and control mechanisms. It is suggested that in the future, immuno-therapeutic measures such as non-specific stimulation of immunological capacity, active and passive immunization or cellular transfer of tumor immunity will be feasible.

- 70-567 METHYLATION OF RIBO- AND DEOXYRIBO-NUCLEIC ACIDS. (Ger.) Schlee, D. (Kirchtor 1, Halle (Saale), Germany). Pharmazie 24(1):1-10, 1969. (170 references)

The physiological significance of the methylated nucleotides found in RNA (especially in transfer and ribosomal RNA) and DNA is discussed. It is suggested that the species-specific patterns of nucleic acid methylation enable the nucleases to distinguish between "self" and "non-self" polynucleotides. Metabolic changes taking place during bacteriophage infection or carcinogenesis may involve changes in RNA and DNA methylation patterns.

- 70-568 CANCER OF THE NASOPHARYNX. (E.) Friedmann, I. Proc. Canad. Otolaryng. Soc. 22:58-65, 1968. (17 references)

Possible explanations for the much higher prevalence of tumors of the nasopharynx among Orientals (especially Chinese) than among Caucasians are discussed. Although no evidence demonstrating a selective effect of inhaled carcinogens on the nasopharynx is presented, it is suggested that environmental factors are of greater importance than genetic factors in the etiology of this tumor.

- 70-569 SMOKING AND LUNG CANCER. (E.) Skinner, E. F. (20 S. Dudley St., Memphis, Tenn.). Med. Trial Techn. Quart. 15(3):59-61, 1969. (13 references)

In the absence of accurate mortality statistics on smoking and true primary lung cancer, it is suggested that any conclusions concerning the causal relationship between smoking and lung cancer are premature and may be erroneous.

- 70-570 NONINDUSTRIAL CHEMICALS AS POSSIBLE FACTORS IN THE ETIOLOGY OF BLADDER CANCER. (E.) Price, J. M. (Abbott Labs., North Chicago, Ill.). J. Nat. Cancer Inst. 43(1):293-294, 1969. (14 references)

Nonindustrial chemicals which may cause bladder cancer in man or other species include tryptophan metabolites, N,N-bis(2-chloroethyl)-2-naphthylamine (an antitumor agent; chlornaphazin), 4-ethylsulfonylnaphthalene-1-sulfonamide, 3-phenyl-5-β-diethylaminoethyl-1,2,4-oxadiazole citrate and N-[4-(5-nitro-2-furyl)-2-thiazolyl]formamide. Further study of nonindustrial chemicals is recommended.

- 70-571 OXIDATION OF CARCINOGENIC AZO-DYES. VI. INFLUENCE OF SUBSTITUTION ON THE CARCINOGENIC ACTIVITY OF AMINOAZOBENZENE. (E.) Marhold, J. (Res. Inst. Organic Synthesis,,

Pardubice-Rybitvi, Czechoslovakia), M. Matrka, V. Rambousek and F. Ruffer. Neoplasma (Bratisl.) 16(2):181-189, 1969. (27 references)

Based on the principles of Druckrey and on data from the authors' experiments and the literature, the carcinogenic activities of numerous derivatives of aminoazobenzene, methylaminoazobenzene, and dimethylaminoazobenzene are quantitatively compared.

70-572 PROBLEMS IN ANIMAL HUSBANDRY CREATED BY THE PRESENCE OF AFLATOXIN IN FEED. (Fr.) Fehr, P. M. (Nat. Inst. Agricult., Paris). Aliment. Vie 56(10-11-12):250-273, 1968. (129 references)

An extensive review includes listings of animals which are highly susceptible, somewhat susceptible and resistant to poisoning by the aflatoxins; the symptoms of poisoning; macroscopic and microscopic lesions which may result; induced metabolic and hematologic disturbances; animal metabolism of these substances; particular effects on immature animals, adult animals and animals being fattened for market; feeds susceptible to contamination; means of preventing contamination; methods for detoxifying contaminated feeds; and max. safe conc. of aflatoxins.

70-573 BLADDER TUMORS IN RATS FED CYCLO-HEXYLAMINE OR HIGH DOSES OF A MIXTURE OF CYCLAMATE AND SACCHARIN. (E.) Price, J. M. Abbott Labs., North Chicago, Ill.), C. G. Biava, J. L. Oser, E. E. Vogin, J. Steinfeld and H. L. Hey. Science 167(3921):1131-1132, 1970. (5 references)

This paper reviews the information presented to the National Academy of Sciences-National Research Council which led to the order that cyclamates be removed from the list of substances generally recognized as safe. In one study, a mixture of sodium cyclamate and sodium saccharin (10:1) was fed to Wistar rats (0-2500 g/kg/day) over a period of about 2 yr. At the 9th week, half the rats were given cyclohexylamine hydrochloride (CHA) equivalent to conversion of 10% of their cyclamate dosage. Papillary tumors of the urinary bladder developed in 8/240 (7 males, 1 female - all receiving 2500 g/kg). Three of the animals with tumors had received CHA. In another study, male and female Charles River-strain albino rats were given 0-15.0 mg of cyclohexylamine sulfate/kg/day. After 2 yr., one male rat of the 17 remaining alive in the high-dose group had a transitional-cell carcinoma of the urinary bladder.

70-574 EDITORIAL: ON THE EPIDEMIOLOGY OF RESPIRATORY DISEASES. (E.) Clemmesen, Scand. J. Resp. Dis. 50(1):52-53, 1969. (no references)

Lung cancer epidemiology and its relationship to smoking and air pollution is discussed.

70-575 VIRAL STATUS OF GERM-FREE RODENTS; PRESENT AND FUTURE. (E.) Kajima, M. (U. Notre Dame Lobund Lab., Ind.). Adv. Exp. Med. Biol. 3:117-124, 1969. (42 references)

Leukemia virus particles (Type C and its precursors) were found in germ-free (GF) mice of 6/6 strains studied; the presence of these particles in fetal tissues suggested vertical transmission of the virus. Mammary tumor virus particles were found in GF C3Hf mice, apparently as the result of vertical transmission. Cisternal Type A tumor virus particles have been found in normal and tumor tissues from GF mice. In contrast to the frequent occurrence of tumor viruses in GF mice, a series of experiments in GF rats failed to demonstrate tumor viruses in normal tissue or in radiation- or carcinogen-induced tumors.

70-576 THE ROLE OF VIRAL INFECTION IN GENITAL CANCERS. (E.) Ravich, A. (47 East 88th St., New York, N. Y.). Cancer Cytol. 8(2):28-35, 1968. (30 references)

Recent findings of virus particles in cervical and prostatic cancer support the concept that a viral carcinogen is present in smegma, and may be transmitted from person to person by sexual intercourse. The clinical evidence is the very low occurrence of genital cancer among Jews as compared to their uncircumcised neighbors in Brooklyn (1.7% and 20%, resp.) a low incidence among the Arab population, who are circumcised at a later age; its virtual absence in nuns; and; a 6-13 times higher prevalence in prostitutes. The occurrence in Jews can be correlated with interethnic sexual relations, and in the case of prostatic cancer, with ascending infection.

70-577 MOLECULAR BIOLOGY OF VIRAL CARCINOGENESIS. (Sp.) Valladares, Y. (City U. Nat. Inst. Oncol., Madrid). Acta Oncol. (Madrid) 8(1):26-55, 1969. (3 references)

Mechanisms of neoplastic transformation and carcinogenesis by DNA- and RNA-containing viruses are discussed and compared to mechanisms of transformation by chemical carcinogens.

70-578 VIRAL ETIOLOGY AND EPIDEMIOLOGY OF LEUKEMIA. (Rus.) Bergol'ts, V. M. (P.A. Herzen Oncol. Inst., Moscow). Vop. Virus. 14(1):5-12, 1969. (36 references)

A review with 9 references to the Russian literature.

70-579 ELECTRON MICROSCOPIC EXAMINATION OF
MURINE LEUKEMIA VIRUSES. (Rus.)

Gogichadze, G. K. (Inst. Exp. Clin. Oncol., Moscow). Probl. Gemat. 14(4):50-54, 1969. (38 references)

A review with only 3 references to the Russian literature.

70-580 CELL TRANSFORMATION BY POLYOMA VIRUS
AND SV40. (E.) Eckhart, W. (Salk

Inst., San Diego, Calif.). Nature (London) 224(5224):1069-1071, 1969. (28 references)

Genotypic and phenotypic changes in cells infected with polyoma virus and SV40 are discussed.

70-581 TUMORS OF THE KIDNEY - PATHOGENESIS.

(Por.) Gentile, A. (U. Gama Filho Sch. Med. Surg., Rio de Janeiro). Bol. Cent. Estud. Hosp. Serv. Estado 20(1-3):3-20, 1968. (97 references)

A review includes sections on genetic factors, epidemiology, associated lesions, experimental studies, the possible role of traumas, and the possible role of viral and other infections.

70-582 IDENTIFICATION OF WOMEN AT HIGH RISK
FOR BREAST CANCER. (E.) Wynder, E. L.

(Sloan-Kettering Inst. Cancer Res., New York, N. Y.). Cancer 24(6):1235-1240, 1969. (24 references)

A review of factors influencing the risk of a woman developing breast cancer.

70-583 THE EPIDEMIOLOGY OF BREAST CANCER;
REVIEW AND PROSPECTS. (E.)

De Waard, F. (U. Utrecht Inst. Social Med., Netherlands). Int. J. Cancer 4(5):577-586, 1969. (51 references)

Geographical variations in breast cancer epidemiology are discussed, with reference to factors contributing to geographical variations in hormonal metabolism patterns.

70-584 EPIDEMIOLOGY AND PATHOLOGY OF CANCER
OF THE THYROID. PART 2: DISCUSSION.

(E.) Farooki, M. A. (Nishtar Med. Coll., Multan Pakistan). Int. Surg. 51(4):317-333, 1969. (163 references)

Worldwide data on the epidemiology and pathology of thyroid carcinoma are compared with information obtained by the author on the basis of 323

surgical cases (from Peshawar, West Pakistan, England including London and Philadelphia, Pa.) and 66 autopsy cases (from Philadelphia), described in Part 1 of this study. The author's data were essentially in agreement with published worldwide data.

70-585 CONSTITUTIONAL DISORDERS OF MAN
PREDISPOSING TO LEUKEMIA AND LYMPHOMA.

(E.) Fraumeni, J. F., Jr. (NCI, Bethesda, Md.). Nat. Cancer Inst. Monogr. 32:221-232, 1969. (82 references)

Evidence is presented to suggest that some diseases associated with chromosomal abnormalities (mongolism; Bloom's, Fanconi's and possibly Klinefelter's and D-trisomy syndromes) are associated with an increased risk of leukemia, whereas congenital disorders of immunity and susceptibility to infection (ataxia-telangiectasia, Wiskott-Aldrich syndrome, agammaglobulinemia, Chediak-Higashi anomaly) are associated with an increased risk of lymphomas. Studies of such "high-risk" populations are recommended for laboratory and epidemiologic research on the leukemias and lymphomas.

70-586 CLINICAL EPIDEMIOLOGY OF LEUKEMIA:

(E.) Fraumeni, J. F., Jr. (NCI, Bethesda, Md.). Seminars Hemat. 6(3):250-260, 1969. (93 references)

The epidemiology of human leukemia as affected by radiation exposure (including the roles of exposure to very low radiation doses before conception or in utero in the epidemiology of childhood leukemia), possible leukemia virus(es), and the presence of inborn disorders (including cytogenetic abnormalities, deficiencies of immunity and familial patterns of disease) are discussed.

70-587 FINITE LIFETIME OF SOMATIC CELLS - A
BASIS OF FINITE LIFESPAN OF ANIMALS.

(E.) Kothari, M. L. (Seth G. S. Med. Coll., Bombay, India) and L. A. Mehta. J. Postgrad. Med. 15(2):53-63, 1969. (55 references)

The non-dividing cells of the body (nerves, muscle, special sensory) are considered to be essentially perennial and ageless, whereas the dividing cells have a 'finite cell-dividing capacity' which is species-specific and definitely age with each division. It is these cells which are responsible for the aging and death of the individual. The longevity of the dividing cell is genetically controlled and at the end of its lifespan, it undergoes senescence (possibly a cellular expression of organismal senescence), then either atrophy or a variant of atrophy, cancer.

PHYSICAL CARCINOGENESIS

70-588 OSTEOGENIC SARCOMA FOLLOWING RADIO-THERAPY FOR RETINOBLASTOMA. (E.) Yoneyama, T. (U. Kentucky Coll. Med., Lexington) and R. H. Greenlaw. Radiology 93(5):1185-1186, 1969.

A 7-mo.-old boy received a max. aggregate dose of 10,700 rad to soft tissue, and 32,260 rad to bone in the area of his left orbit during treatment for a retinoblastoma. At about 2.5 yr. of age, the eye was enucleated because of a secondary glaucoma. At the age of 17 yr., swelling in that region was noted and biopsy revealed an osteogenic sarcoma. The pt. died 20 mo. after this diagnosis, 16.5 yr. after radiotherapy.

70-589 RETICULAR NEOPLASMS IN IRRADIATED AND UNIRRADIATED GERM-FREE MICE. (E.) Walburg, H. E., Jr. (Oak Ridge Nat. Lab., Tenn.) and G. E. Cosgrove. Adv. Exp. Med. Biol. 3:135-141, 1969.

Spontaneous myeloid leukemias did not develop in germ-free (GF), conventional (C) or conventionalized (Cz) mice of 3 strains (inbred RFM or AKR, non-inbred ICR). After X-irradiation (300 r), myeloid leukemias developed in C and Cz mice, but not in GF mice. All irradiated groups showed more thymic and non-thymic lymphomas, and fewer reticulum cell sarcomas (this reduced frequency was attributed to a reduced survival time), than non-irradiated mice. Thymic lymphomas were more frequent in both irradiated and non-irradiated GF mice than in irradiated or non-irradiated C or Cz mice; non-thymic lymphomas, however, were no more frequent (sometimes less frequent) in GF mice than in C or Cz mice. No significant difference was seen between GF mice and C or Cz mice in the total incidence of radiation-induced tumors (lymphomas and myeloid leukemias). By comparison to C mice, the GF mice showed an accelerated death rate, beginning at age 200 days in males and age 300 days in females.

0-590 THE EFFECTS OF RADIATION ON CHROMOSOMES OF BONE MARROW CELLS. I. TYPE AND FREQUENCY OF RAT CHROMOSOME ABERRATIONS INDUCED BY FAST NEUTRONS, X-RAYS AND GAMMA RAYS. (E.) Kamada, N. (Hiroshima U. Res. Inst. Nucl. Med. Biol., Japan). Acta Haemat. Jap. 32(2):212-235, 1969.

Bone marrow cells were obtained from female Sprague-Dawley rats 3 hours-10 mo. after irradiation (200 rads of fast neutrons, γ -irradiation or X-rays). High frequencies of unstable chromosomal aberrations (Cu), predominantly chromatid breaks and exchanges, were seen shortly after irradiation, but the frequencies of Cu decreased rapidly in the first 3 days after irradiation. Nearly 1 of the chromosomal aberrations observed 1-10

mo. after irradiation (involving 1.73-2.7% of the cells, depending on the type of radiation admin.) were stable forms (Cs), such as deletions and translocations. The frequencies of Cs, and the frequency of translocations observed among the Cs, were higher in rats exposed to fast-neutron irradiation than in rats exposed to the other 2 types of radiation. Clones of cells containing Cs (5-15% of the cells examined) were found in the bone marrows of 4 rats. The chromosomal aberrations observed shortly after irradiation originated mainly from the erythroblasts.

70-591 THE EFFECTS OF RADIATION ON CHROMOSOMES OF BONE MARROW CELLS. II. STUDIES ON BONE MARROW CHROMOSOMES OF ATOMIC BOMB SURVIVORS IN HIROSHIMA. (E.) Kamada, N. (Hiroshima U. Res. Inst. Nucl. Med. Biol., Japan). Acta Haemat. Jap. 32(2):236-248, 1969.

Bone marrow cells were obtained from 47 healthy persons (without malignant, infectious or viral diseases) exposed 20 yr. previously to the Hiroshima atomic bomb (within 3000 meters of the hypocenter) and from 17 non-exposed healthy controls. None of the subjects had been exposed to other forms of irradiation except single chest X-rays. Differential bone marrow counts were the same in most exposed persons as in controls, although persons exposed within 1500 meters of the hypocenter showed an increase in bone marrow plasma cells. Moderate anemia and leukopenia were somewhat more frequent among the exposed persons than among the controls. Bone marrow preparations from the exposed and non-exposed persons showed the same frequencies of aneuploid cells; no radiation-induced chromosomal aberrations (rings, fragments, dicentric or exchanges) were found in either group.

70-592 THE EFFECTS OF RADIATION ON CHROMOSOMES OF BONE MARROW CELLS. III. CYTOGENETIC STUDIES ON LEUKEMIA IN ATOMIC BOMB SURVIVORS. (E.) Kamada, N. (Hiroshima U. Res. Inst. Nucl. Med. Biol., Japan). Acta Haemat. Jap. 32(2):249-274, 1969.

The Ph^1 chromosome was found in bone marrow cells from 18/18 pts. with chronic granulocytic leukemia (CGL). Frequencies of Ph^1 were not correlated to peripheral WBC levels, neutrophilic alkaline phosphatase (NAP) values or the effects of therapy. The 8 previously radiation-exposed (RE) pts. (1/8 to radiotherapy for cancer, 7/8 to the Hiroshima atomic bomb) tended to show a milder course of the disease. Whether this milder course was peculiar to radiation-induced leukemia, or whether it was an age-related phenomenon (the estimated mean ages at onset in RE and non-exposed pts. were 55.1 and 41 yr.,

resp.), could not be determined. Clinical and laboratory findings in 3 non-exposed (NE) pts. with CGL in acute transformation were similar to those seen in 1 RE pt. In 26 NE and 10 RE pts. with acute leukemia, estimated mean ages at onset were 40.4 and 51.2 yr., resp. Clinical, physical and laboratory findings were similar in both groups, and no significant differences in survival time were noted. Aneuploidy was about equally frequent in bone marrow cells from RE and NE pts. No abnormalities common to all pts. were seen in cells from the 6/10 RE pts. showing chromosomal abnormalities; however, a common chromosomal anomaly (deletion or translocation of a Group G chromosome) was found in cells from 6/10 NE pts. showing chromosomal abnormalities. These 6 pts. also showed low NAP values. No evidence indicating a high frequency of aleukemic leukemia was noted among the RE pts. with acute leukemia.

70-593 PRIMARY CARCINOMA OF THE TRACHEA FOLLOWED BY PRIMARY CARCINOMA OF THE ESOPHAGUS AFTER A SIX-YEAR INTERVAL. A CASE REPORT. (E.) Senyszyn, J. J. (NIH, Bethesda, Md.) and H. W. Jacox. Radiology 92(6):1346-1348, 1969.

A 64-yr.-old man with a primary squamous cell carcinoma of the lower third of the trachea, treated with a mid-plane dose of 4300 rads through anteroposterior and posteroanterior 10 x 15 cm. ports, died 6 yr. later of a squamous cell carcinoma of the mid-esophagus. Autopsy revealed a primary prostatic carcinoma as well as the esophageal carcinoma, but no evidence of recurrent tracheal carcinoma. The possibility that the second primary tumor was a complication of the previous radiotherapy was regarded as unlikely.

70-594 PRECANCEROUS DISEASES OF THE LIPS. (Ger.) Maškillejson, A. L. (Med. Inst. Stomat., Moscow). Derm. Mschr. 155(2):103-113, 1969.

The clinical picture and histology of 3 forms of precancerous lesions of the red lip curve are described: 1) cheilitis abrasiva cancerosa Manganotti which was seen in 47 pts. (41 men, 6 women, duration of disease 2 mo.-7 yr.); 42/47 were > 50 yr. old, 7/47 also had extensive glandular cheilitis, in 6/47 it was preceded by trauma, in 2/47 by a herpes infection and in 20/47 malignant degeneration occurred; 2) a nodular form (frequently misdiagnosed as papilloma or small warts) was seen in 25 pts. (22 men, 3 women, duration 3 mo.-5 yr.); 15/25 were > 40 yr. old, in 4/25 it developed after trauma, in

2/25 after herpes, malignant transformation occurred in 13/25; 3) circumscribed hyperkeratosis which was seen in 31 pts. (26 men, 5 women, duration 6 mo.-7 yr.); in 2/31 it was preceded by trauma, 1/31 by herpes, 4/31 also had glandular cheilitis, malignant transformation occurred in 9/31. The precancerous lesions were localized on the lower lip in 97/103; 64/97 worked outdoors (influence of sunlight on pathogenesis). One of the first indications of malignant transformation was the disappearance of the PAS-positive area in the basal membrane. Comparison of the three forms showed that the histological changes of the proliferating parts of the epidermis were generally the same in spite of the great differences in clinical picture. The histological changes of the upper parts of the epidermal layer differed and corresponded with clinical picture: erosion in abrasive precancerous cheilitis, proliferation to the top (but not as in papilloma) in nodular form and hornification in hyperkeratosis.

70-595 CARCINOMATOUS CHANGES IN LUPUS VULGARIS. (E.) Förström, L. (Univ. Cent. Hosp., Helsinki). Ann. Clin. Res. 1(3):213-219, 1969.

Malignant transformation was found in 38/460 pts. with lupus vulgaris at the University Central Hospital in Helsinki, between 1947 and 1966: 27 squamous cell carcinomas, 11 basal cell carcinomas and 4 pts. with senile keratosis. The ages of the cancer pts. ranged from 35-75 yr., the av. (52) being 7 yr. more than the entire group, and the development of malignancy occurred about 35 yr. after the onset of lupus. The av. age of pts. with senile keratosis was 56 yr., with a 43-yr. latent period. The areas of transformation were mainly those exposed to the sun, as were the initial lesions of lupus, but the incidence was not higher in outdoor workers. Treatment with X-rays (especially in combination with caustic chemicals) was proposed as an important factor in carcinogenesis.

70-596 DEGENERATED ULCER AND ULCERATED CANCER OF THE STOMACH. (Fr.) Chatelin, C. L. (Princess Grace Welcome Ctr., Monaco). Sem. Hop. Paris 45(18):1163-1167, 1969.

The difficulties of diagnosis of stomach cancer developing from duodenal ulcers are illustrated by 2 case histories.

See also abstract nos.: 558,561,586,818,939

CHEMICAL CARCINOGENESIS

70-597 ELECTRONIC PROPERTIES OF N-HETERO-AROMATICS. XL. A NUCLEAR MAGNETIC RESONANCE STUDY OF THE INTERACTION OF 4-NITROQUINOLINE 1-OXIDE WITH DEOXYRIBONUCLEOSIDES. (E.) Okano, T. (Tohoku U. Sch. Med., Sendai, Japan), A. Takadate and T. Kano. Gann 60(5): 557-568, 1969.

The effects of the presence of the carcinogen 4-nitroquinoline-1-oxide on the proton chemical shifts of deoxyribonucleosides and related compounds were studied in deuterated dimethyl sulfoxide. The carcinogen caused an up-field shift of signals of the ring and amino protons of purine deoxyribonucleosides and the NH proton of deoxythymidine, a small down-field shift of the C-1, H triplet of deoxythymidine, and no alterations in proton spectra of pyrimidine nucleosides. The shifts depended on the conc. of the carcinogen. The difference absorption spectra of mixtures of the carcinogen and purine deoxyribonucleosides are presented.

70-598 ELECTRON SPIN RESONANCE STUDY ON THE FREE RADICALS PRODUCED FROM CARCINOGENIC MINONAPHTHOLS AND N-HYDROXY-AMINONAPHTHALENES. (E.) Nagata, C. (Nat. Cancer Ctr. Res. Inst., Tokyo), Y. Ioki, M. Inomata and A. Imamura. Gann 60(5):509-522, 1969.

Of 12 aromatic amines and naphthols studied by the electron spin resonance method, the known carcinogens 2-amino-1-naphthol, 1-amino-2-naphthol, N-hydroxy-1-aminonaphthalene, and N-hydroxy-2-aminonaphthalene produced abundant free radicals in organic solvents and water, whereas the noncarcinogenic aromatic amines and naphthols did not release free radicals, with the exception of 4-amino-1-naphthol. The pH influenced production of free radicals, which differed in kind in acidic and alkaline solutions. The relation between free radical production and carcinogenesis by aromatic amines is discussed.

70-599 NMR CHEMICAL SHIFTS IN CARCINOGENIC POLYNUCLEAR HYDROCARBONS. (E.) Bartle, K. D. (U. Bradford Sch. Chem., England), W. Jones and R. S. Matthews. J. Med. Chem. (6):1062-1065, 1969.

Recently measured chemical shifts, observed in high-field nuclear magnetic resonance spectra of certain polycyclic aromatic hydrocarbons, were used to assess the validity of LCAO calculations underlying some theories of carcinogenesis. Small discrepancies between observed and calculated values are discussed in terms of molecular geometry.

70-600 EXPERIMENTAL BIOSYNTHESIS OF POLY-BENZENOID HYDROCARBONS OF THE 3,4-

BENZOPYRENE TYPE IN RELATION TO FOREST SOILS. (Fr.) Mallet, L. and M. Tissier. C. R. Soc. Biol. (Paris) 163(1):63-65, 1969.

Soil from a park near Paris contained 80-100 µg 3,4-benzpyrene/100 g in its natural state. When sterilized, sown with Clostridium putride, and allowed to remain at room temperature for 4 mo., it yielded 160 µg/100 g. When cultured for 6 mo. under anaerobic conditions, following similar preparation, soil from a woodland at a considerable distance from any industrial area yielded up to 4.2 µg/100 g, as compared to less than 1-2 µg/100 g, prior to sterilization. In the presence of E. coli, similar results were obtained. When the fatty acids contained in the untreated soil were extracted with benzene and the benzpyrene-free extract was evaporated, mixed with a small amount of acetone, and added to a soft gel medium sown with C. putride, small quantities of 3,4-benzpyrene were demonstrable after 4 mo. of anaerobic culturing at 31° C, although control cultures not receiving C. putride yielded no hydrocarbons.

70-601 BIOSYNTHESIS OF 3,4-BENZOPYRENE AND ANAEROBIOSIS. (Fr.) Brisou, J. (Lab. Microbiol., Poitiers, France). C. R. Soc. Biol. (Paris) 163(3):772-774, 1969.

Following the addition of pentadecanoic, margaric, or eicosanoic acid, traces of 3,4-benzpyrene were produced by cultures of Welchia and Clostridium grown for unspecified periods of time at 37°C, under anaerobic conditions, in a brain-heart broth or a reducing medium containing thioglycollate; measurable amounts were produced in the presence of nonadecanoic acid, sodium oleate, or an unspecified mixture of estrogens ("Equigyne"); none, in the presence of thioglycollate alone, cholesterol, or a combination of p-aminobenzoic acid and succinic anhydride. Other unspecified, microbial strains, cultured in the presence of sodium palmitate or squalene, produced appreciable amounts of substances with chromatographic peaks at 380 and 390, presumably representing polybenzenoid hydrocarbons close to 3,4-benzpyrene.

70-602 CARCINOGENIC SUBSTANCES IN WATER AND SOIL. XXV. ANIMAL TESTS ON CARCINOGENICITY OF CHLORINE DERIVATIVES OF 3,4-BENZOPYRENE. (Ger.) Müller, E. (U. Mainz Inst. Hyg., Germany) and J. K. Reichert. Arch. Hyg. Bakt. 153(1):26-32, 1969.

The biological activity of 5,8,10-trichloro-3,4-benzpyrene, 5 chloro-3,4-benzpyrene and 5,8,10-trichloro-3,4-benzpyrene-1,2,6,7-tetrachloride was tested in groups (25 animals each) of 3-mo.-old female NMRI mice either by s.c. inj. (10 mg in 12 biweekly inj.) or percutaneous (painting)

application (10 mg in 50 applications over 25 weeks). The animals were observed for 532 days. In 4/200 mice malignant tumors developed, but the latent periods and localization indicated that their occurrence was not related to the application of these compounds. It is concluded that these substances are not carcinogenic. Since they are derivatives of 3,4-benzpyrene obtained after chlorine dioxide treatment of drinking water, it is suggested that this procedure eliminates not only bacteria and viruses but also carcinogens.

70-603 CARCINOGENICITY OF POLLUTED AIR: III. A RADIOACTIVE TRACER TECHNIQUE FOR QUANTITATIVE DETERMINATION OF POLYCYCLIC AROMATIC HYDROCARBONS. (It.) Candeli, A. (U. Perugia, Italy) and G. Morozzi. Gior. Ig. Med. Prev. 10(1):3-15, 1969.

In a series of column and paper chromatographic studies, the percentage recovery of ^3H -3,4-benzpyrene (BP) in quantitative analysis of a mixture of the tritiated BP with a group of other polycyclic aromatic hydrocarbons (1,2-benzpyrene, unlabeled BP, 1,2,5,6-dibenzanthracene, coronene, 3-methylcholanthrene and 1,2,5,6-dibenzacridine) corresponded to the percentage recovery of both unlabeled BP and the other hydrocarbons within acceptable statistical limits for this type of study. Losses for all compounds during column chromatography were of the order of 30%-35%; during paper chromatography, they were of the order of 50%. The addition of ^3H -BP in a quantity sufficient to yield 150,000 cpm at the start of the experiment appeared to be sufficient to give a reliable internal standard for studies of this kind. During column chromatographic analysis of the particulate content of exhaust fumes from an automobile engine, the loss of added ^3H -BP was 31.70%, as determined by liquid scintillation counting at the beginning and end of the analysis. Thirteen polycyclic, aromatic hydrocarbons were identified and 10/13 were quantified by spectrophotometric analysis of the particulate matter in question.

70-604 CARCINOGENIC SUBSTANCES IN COOKING FAT AND OIL. VI. FURTHER STUDIES ON MARGARINE AND CHOCOLATE. (Ger.) Fábian, B. (U. Mainz Inst. Hyg., Germany). Arch. Hyg. Bakt. 153(1):12-24, 1969.

Analysis of 8 samples of different margarines revealed that the content of carcinogenic aromatic compounds (1,2-benzanthracene, 3,4-benzfluoranthene, 3,4-benzpyrene, indeno[1,2,3-cd]pyrene and 10,11-benzfluoranthene) was substantially lower (2-4 $\mu\text{g}/\text{kg}$) in brands which during manufacture had been treated with activated charcoal and steam than in untreated margarines (20-100 $\mu\text{g}/\text{kg}$). Five chocolate samples analyzed contained approx. 6 $\mu\text{g}/\text{kg}$ of these substances.

70-605 FURTHER STUDIES ON THE TUMOR-INHIBITORY AND TUMOR-INDUCING PROPERTIES OF N-ISOPROPYL- α -(2-METHYLHYDRAZINO)-p-TOLUAMIDE HYDROCHLORIDE (PROCARBAZINE HYDROCHLORIDE). (E.) Grunberg, E. (Hoffmann-La Roche Inc., Nutley, N. J.) and H. N. Prince. Chemotherapy (Basel) 14(2):65-76, 1969.

The carcinogenic effects of procarbazine HCl (P; ibenzmethylin; 1 dose/week for up to 8 weeks) were studied in CD-1 Swiss mice, CD albino rats and Syrian golden hamsters. In the mice, P induced lung tumors in 23%, 55% and 72% after 8, 12 and 21 weeks of observation, resp. No clear dose-effect relationship was seen at the doses used (100-500 mg/kg). No other grossly visible lesions were found. In the rats, admin. of P (100-500 mg/kg i.p. or p.o.) induced s.c. tumors in 14% and 33% after 12 and 21 weeks of observation, resp.; no tumors developed in rats observed for 8 weeks. Tumors were more frequent in female rats than in males. No other organs showed gross lesions. In both mice and rats, P was a more effective carcinogen when admin. p.o. than when admin. i.p. In the hamsters, admin. of P (100-500 mg/kg x 3-8 i.p. or p.o.) did not induce tumors. High doses of P had hypnotic effects in all 3 species.

70-606 CARCINOGENICITY OF A RUBBER ADDITIVE. (E.) Carter, R. L. (Chester Beatty Res. Inst., London) and F. J. C. Roe. Food Cosmet. Toxic. 6(6):823-824, 1968.

The rubber additive "Curetard" (polymerized N-nitroso-2,2,4-trimethyl-1,2-dihydroquinoline; NTDQ) was admin. in 20-week courses to 6-7-week-old Sprague-Dawley rats. More than 80% of the rats of both sexes survived 80 weeks; after that time, several females developed mammary tumors and were sacrificed. After s.c. admin. (1 inj./week of 25 mg, total 500 mg), NTDQ induced grossly visible inj. site tumors in 6/20 males and 3/20 females; microscopic tumors were detected in 14/20 and 6/20, resp. After i.p. admin. (same regimen as with s.c. admin.), no grossly visible peritoneal tumors were seen, but microscopic tumors developed in 2/20 males and 1/20 females. After force-feeding of NTDQ (3 doses/week of 25 mg, total 1500 mg), the tumor incidence was the same as in untreated or vehicle-treated controls. No bladder tumors were seen in any of the treated rats. It is suggested that since NTDQ had no apparent activity when admin. p.o. to rats, the risk of occupational exposure to this compound in man is not likely to be serious.

70-607 PRELIMINARY SURVEY OF 22 PRINTING INKS FOR CARCINOGENIC ACTIVITY BY THE SUBCUTANEOUS ROUTE IN MICE. (E.) Carter, R. L. (Chester Beatty Res. Inst., London), B. C. V. Mitchley and F. J. C. Roe. Food Cosmet. Toxic. 7(1):53-58, 1969.

Male CB stock mice were treated s.c. for 15-22 week (1 inj./week) with 22 printing inks of unspecified composition. No inj. site tumors were seen in mice admin. 17/22 inks, and the types and incidences of other tumors were the same as in controls. Inj. site tumors developed in 1/20 mice of each group treated with the other 5 inks. These inj. site tumors developed after long latent periods (18-19 mo.) in the mice admin. 4 of these inks; 1 additional animal among the groups admin. 2/4 of these inks developed adenocarcinomas of the lung. One mouse treated with the fifth ink developed an anaplastic sarcoma of the inj. site after 7 mo., another mouse developed a large retroperitoneal spindle cell sarcoma, but no inj. site tumor. Survival times in mice treated with this ink were poor.

70-608 NON-CARCINOGENICITY OF HEXAMETHYLENE-TETRAMINE IN MICE AND RATS. (E.)

Della Porta, G. (Nat. Inst. Study Cure Tumors, Milan, Italy), M. I. Colnaghi and G. Parmiani. Food Cosmet. Toxic. 6(6):707-715, 1968.

Hexamethylenetetramine (HMT; formerly proposed as an antimicrobial agent in foods) was admin. to 5-7-week-old mice of 2 inbred strains (C3Hf/Dp or SWR/Dp) as a 1% soln. in the drinking water for 60 weeks. Mice of an outbred strain (CTM; 10 weeks old) received 1% or 0.5% HMT for 60 weeks, or 5% HMT for 30 weeks. Wistar rats (10 weeks old) received 1% HMT for 104 weeks or 5% HMT for 2 weeks. One group of 10-day-old CTM mice and 1 group of 10-day-old Wistar rats received 5 s.c. inj. of HMT (5 g/kg on alternate days). All animals were observed throughout life. No evidence of carcinogenic activity was seen in any of the treated groups. The only group showing an adverse effect of HMT on growth or survival was the group of rats admin. the 5% soln.; in this group, the mortality rate was 50% after 2 weeks.

70-609 CARCINOGENICITY OF PONCEAU MX IN THE MOUSE. (E.) Grasso, P. (Brit.

Indust. Biol. Res. Ass., Carshalton, Surrey, England). Food Cosmet. Toxic. 6(6):821-822, 1968.

It is suggested that the "hepatocellular carcinomas" previously described in mice fed Ponceau MX (a food coloring) were not true neoplasms, but rather lesions of regenerative hyperplasia with some unusual morphologic characteristics.

70-610 NITROSAMINES IN WHEAT FLOUR. (E.)

Thewlis, B. H. (Flour Milling Baking Res. Ass., St. Albans, Hertfordshire, England). Food Cosmet. Toxic. 6(6):822-823, 1968.

The characteristics of a diethylnitrosamine (DENA) spot on a thin-layer chromatogram are

compared to the properties of another spot, surrounding the DENA spot and showing about the same R_f value as DENA, which might have arisen from some reaction with phenols present in the wheat flour sample and traces of atmospheric nitrite. Similar spots were produced in chromatograms of other substances, such as p-nitrosophenol, 1-nitroso-2-naphthol, caffeic acid and synthetic 1-caFFEYL glycerol. It is suggested that previously published reports of DENA in certain wheat flour samples may have resulted from an analytical error of this type.

70-611 COMPARISON BETWEEN THE EFFECTS OF A SINGLE DOSE OF A CHEMICAL CARCINOGEN ON GNOTOBIOTIC AND CONVENTIONAL MICE. (E.)

Grant, G. A. (Chester Beatty Res. Inst., London) and F. J. C. Roe. Adv. Exp. Med. Biol. 3:143-146, 1969.

Germ-free (GF) and conventional (C) 7-day-old C3H mice were inj. s.c. with heat-sterilized 7,12-dimethylbenzanthracene (25 µg). At age 36 weeks, 7/29 GF mice (24%) and 18/48 C mice (37%) had developed sarcomas at the inj. site. The tumor incidence was significantly higher in the C mice than in the GF mice at ages 24-28 weeks (inclusive). All treated male mice (C or GF) observed for 30 weeks or more developed hepatomas, as did 1 untreated C male and 1 treated GF female; 5 mice (1 GF female, 3 C females, 1 C male) also developed adenomas of the lung. In 5-week-old GF or C mice inj. i.m. with 3-methylcholanthrene (50 µg), the incidence of inj. site sarcomas 19 weeks later (20/26 GF mice, 24/25 C mice) was about the same in both groups. The latent period for tumor development in both groups was about 10 weeks. It is concluded that this carcinogen dose exceeded the optimal level. The results suggested that the absence of bacteria and horizontally-transmitted virus can affect the carcinogenic actions of chemicals in marginal doses.

70-612 INFLUENCE OF CARCINOGENS AND GROUP-SPECIFIC COMPOUNDS ON DNASE II. (E.)

Melzer, M. S. (U. Guelph, Ontario, Canada). Canad. J. Biochem. 47(10):987-989, 1969.

DNase II (hog spleen) activity was 93-99% suppressed after incubation for 17 hours at 38°C with either iodoacetic acid (additive/enzyme molar ratio (A/E) greater than 1000, N-bromosuccinimide (A/E 24 or more, incubated for 30 min.), or hydrogen peroxide (A/E greater than 10,000). A 30% loss of activity was seen after treatment with iodoacetamide. Activity was decreased less than 10% after exposure to several carcinogens (diepoxybutane, β-butyrolactone, 3-hydroxyxanthine and ascaridole), malonaldehyde and diisopropylfluorophosphate. It is concluded that the carcinogens may not act directly on DNase II (at least in their non-metabolized forms) in the critical reaction of carcinogenesis, but that tryptophan,

methionine and/or histidine residues have important roles in the activity of DNase II.

- 70-613 RESPONSE TO 4-DIMETHYLAMINOAZOBENZENE (DAB) OF MAMMALIAN CELLS IN CULTURE. (E.) Takaoka, T. (U. Tokyo, Japan), H. Katsuta, S. Ohta, M. Miyata, A. Hosokawa and M. Furuya. Jap. J. Exp. Med. 38(4):259-268, 1968.

The results of 6 days of incubation with 4-dimethylaminoazobenzene (DAB; 1-10 µg/ml) were studied in several types of cell cultures. Normal rat liver cells (strains RLC-4, -5, -7 and -10) showed a dose-related inhibition of cell proliferation. In RLC-10, a young culture (34 days), all conc. of DAB induced cell destruction; large inocula of RLC-5 were resistant. In strains of rat ascites hepatoma cells originally induced by DAB feeding (JTC-2, AH-7974TC and AH-66TC), all but the AH-66TC strains were very resistant. Normal rat epithelioid cells and L-929 mouse fibroblasts were less sensitive to DAB-induced inhibition of proliferation, as were rat liver cells transformed by "NAGISA" culture (strain RLH-1). Tween 20 (0.005-0.05%) increased the cytopathogenic effect of DAB on RLC-7 and JTC-2 cells.

- 70-614 IMMUNOSUPPRESSION AND CARCINOGENESIS: CONTRASTING EFFECTS WITH 7,12-DIMETHYLBENZ[a]ANTHRACENE, BENZ[a]PYRENE, AND 3-METHYLCHOLANTHRENE. (E.) Ball, J. K. (U. Western Ontario Cancer Res. Lab., Canada). J. Nat. Cancer Inst. 44(1):1-10, 1970.

In newborn CFW/D mice, 7,12-dimethylbenzanthracene (DMBA; 60 µg s.c.), but not carcinogenic doses of 3,4-benzpyrene or 3-methylcholanthrene, suppressed both primary and secondary immune responses to sheep RBC; the primary hemolysin response was suppressed in a dose-dependent fashion by as little as 6 µg DMBA neonatally. Neonatal DMBA immunosuppression was correlated with a high incidence of tumors of lymphatic tissue. In adult mice, a carcinogenic dose of DMBA (1 mg i.m.) delayed the max. hemolysin response for only 1 day.

- 70-615 EFFECT OF KREBS CYCLE METABOLITES ON THE GROWTH OF MFS8 CELLS CULTIVATED IN VITRO. Shirodkar, A. S. (Cancer Res. Inst., Bombay, India) and B. N. Mashelkar. Indian J. Med. Res. 57(1):164-166, 1969.

The metabolites cis-aconitic acid, α -ketoglutaric acid, sodium citrate, sodium fumarate, sodium maleate, sodium pyruvate, sodium succinate, and oxalacetic acid, but not cis-isocitric acid, promoted the in vitro growth of a variant of MFS8 (derived from a mouse fibrosarcoma) cells, in optimum conc. ranging from 1-5 mM. Oxalacetic acid (1 mM) exerted the most pronounced effect.

- 70-616 REACTION MECHANISM OF 4-HYDROXYAMINOQUINOLINE 1-OXIDE AND RELATED COMPOUNDS IN INACTIVATION OF THE TRANSFORMING ACTIVITY OF DEOXYRIBONUCLEIC ACID. (E.) Tanooka, H. (Nat. Cancer Ctr. Res. Inst., Tokyo), Y. Kawazoe and M. Araki. Gann 60(5):537-543, 1969.

The effectiveness of 4-hydroxyaminoquinoline (4-HAQ) in inactivating the transforming ability of B. subtilis DNA was greater than that of certain hydroxyamino derivatives of quinoline and pyridine. The addition of organic solvents such as ethanol or of various DNA substituents to the reaction medium containing DNA and 4-HAQ protected the DNA from inactivation. It is suggested that 4-HAQ inactivates DNA through an intermediate free radical, which acts on a number of DNA sites and is inhibited competitively by the organic solvents.

- 70-617 EFFECT OF 7,12-DIMETHYLBENZ[a]ANTHRACENE AND SPLENECTOMY ON VIRUS TITER AND BLOOD PICTURE IN FRIEND VIRUS LEUKEMIA. (E.) Elliott, S. C. (Drake U., Des Moines, Iowa), W. K. Kiehn, C. A. Reilly, Jr. and G. T. Schloss. Proc. Soc. Exp. Biol. Med. 133(2):529-535, 1970.

In adult BALB/c mice inoc. with Friend virus, weekly painting with 7,12-dimethylbenzanthracene (DMBA, beginning at the time of inoc.) delayed neoplastic transformation of splenic reticulum cells, decreased splenic virus titer, improved the blood picture, ameliorated hepatosplenomegaly, and prolonged the survival time. Splenectomy in mice subsequently inoc. with Friend virus also increased the survival time but, when combined with DMBA treatment, rapidly led to a profound, fatal anemia.

- 70-618 ONCOGENIC PURINE DERIVATIVES: EVIDENCE FOR A POSSIBLE PROXIMATE ONCOGEN. (E.) Stöhrer, G. (Sloan-Kettering Inst. Cancer Res., New York, N. Y.) and G. B. Brown. Science 167(3925):1622-1624, 1970.

Two additional urinary metabolites of the carcinogen 3-hydroxyxanthine, 8-chloroxanthine and 8-methylmercaptioxanthine, were identified in Wistar and Sprague-Dawley rats by ion exchange and subsequent paper chromatography. The 2 metabolites were reducible to xanthine in vitro with no loss of specific activity; the identity of 8-chloroxanthine was further confirmed by the recovery of urinary 8-(³⁶Cl)chloroxanthine after feeding Na³⁶Cl along with 3-hydroxyxanthine. The 2 metabolites were thought to be derived from a reactive intermediate, which may be a proximate carcinogen.

- 70-619 EFFECT OF CARCINOGENIC SUBSTANCES ON IN VITRO REPLICATION AND TRANSCRIPTION OF DEOXYRIBONUCLEIC ACIDS. EFFECT OF

BROMOMETHYLATED AROMATIC HYDROCARBONS. (Fr.) Daudel, P. (Inst. Nucl. Phys. Curie Lab., Paris), F. Lucher, M. Croisy-Delcey, J. Moreau, P. Jacquignon and N. P. Buu-Hoi. *C. R. Acad. Sci. [D] (Paris)* 270(19):2394-2396, 1970.

The *in vitro* incorporation of ^{14}C -labeled adenosine triphosphate into a system containing RNA polymerase (fraction V, derived from *Micrococcus lysodeikticus*), 3 non-radioactive nucleotides (CTP, GTP, UTP), calf thymus DNA, spermidine hydrochloride and manganese chloride was evaluated by determining the amount of radioactivity incorporated in an acid-insoluble precipitate, expressed as a function of the time of incubation. The control system contained acetone soln. alone; the test systems contained 9-bromomethylanthracene (BMA) or 7-bromomethylbenzanthracene (BMBA), both in acetone soln. The non-carcinogenic homolog (BMA) inhibited incorporation only slightly, while the strongly carcinogenic compound (BMBA) inhibited it by almost 70% after 10 min. incubation.

70-620 OBESITY INDUCED IN MICE INJECTED INTRACEREBRALLY WITH 4-NITROQUINOLINE 1-OXIDE OR 4-HYDROXYAMINOQUINOLINE 1-OXIDE. (E.) Yamamoto, S. (Inst. Physical Chem. Res., Saitama, Japan), T. Mizutani, C. Kaneuchi and Y. Shirasu. *Proc. Soc. Exp. Biol. Med.* 133(1):303-306, 1970.

Female albino ddOM mice (genetically nonobese) were given a single, unilateral, intracerebral inj. of various conc. of 4-nitroquinoline 1-oxide (NQO), 4-hydroxyaminoquinoline 1-oxide (HAQO), and 4-aminoquinoline 1-oxide (AQO) in an effort to induce brain tumors. By 3 days, a marked increase in food and water intake followed by a steep rise in body wt. was noted in groups given 0.2% NQO or 0.05% HAQO. Body wt. increased to 60 g as compared to control groups whose mean wt. ranged from 23-27 g; the HAQO group being significantly higher. Dietary restriction of food resulted in wt. loss, which was regained with resumption of free feeding. Autopsy revealed marked fat deposits, especially in the abdominal cavity and necrosis of nerve cells in the dorsolateral region of Ammon's horn in the injected side. No obesity could be induced with: 3,4-benzpyrene, β -propiolactone, N-nitrosomethylurea, or N-hydroxy-N-2-fluorenyl-acetamide.

70-621 METABOLIC STUDIES ON MECHANISM OF URETHAN ACTION. IV. INFLUENCE OF URETHAN ON NUCLEIC ACID METABOLISM IN RAPIDLY PROLIFERATING TISSUES *IN VIVO*. (E.) Giri, C. P. (Cancer Res. Inst., Parel, Bombay, India) and S. V. Bhide. *J. Nat. Cancer Inst.* 43(5): 1103-1107, 1969.

In 8-10-week-old partially hepatectomized male Swiss mice, and in mice of the same age bearing transplanted fibrosarcomas, treatment with

urethan (U; 1 mg/g) had no effect on DNA or RNA levels in the tumor tissue or in regenerating liver, although both tissues showed a decrease in aspartic transcarbamylase activity. Treatment with U increased acid DNase and (to a lesser extent) RNase activities in lung and (to a lesser extent) liver tissue from normal newborn or adult mice, but had no effect on DNase or RNase in tumor tissue and regenerating liver. It is concluded that the effects of U on various aspects of nucleic acid metabolism are apparently not the sole expression of a mechanism of U carcinogenesis.

70-622 INFLUENCE OF SPLENECTOMY ON INTRA-VENOUSLY INDUCED AND SPONTANEOUS METASTASES IN MICE. (E.) Boeryd, B. (U. Goteborg, Sweden) and B. Hagmar. *Path. Europ.* 4(1):12-17, 1969.

The effects of heparin (H) or epsilon-aminocaproic acid (EACA) on the formation of lung and liver metastases were studied in intact or splenectomized (splx.) mice inj. i.v. with cells from a syngeneic 3-methylcholanthrene-induced rhabdomyosarcoma. Splx. mice showed a lower frequency of liver metastases (but not of lung metastases) than intact mice. Admin. of H and EACA reduced and increased, resp., the frequencies of liver and lung metastases in intact mice. Splx. did not modify the effects of EACA, but H-treated splx. mice showed a higher frequency of lung metastases than H-treated intact mice. The formation of spontaneous lung and liver metastases from resectable tumors was enhanced by splx.

70-623 CYTOTOXIC EFFICIENCY AND EFFECT ON TUMOUR GROWTH OF HETEROSPECIFIC ANTILYMPHOCYTIC AND ANTITUMOUR SERA. (E.) Woodruff, M. (U. Edinburgh) and L. H. Smith. *Nature (London)* 225(5230):377-379, 1970.

Rabbit or horse antilymphocyte serum (ALS) and globulin (ALG) against mouse thymocytes were cytotoxic for mouse mammary carcinoma, a methylcholanthrene-induced sarcoma, and lymphocytes *in vitro*, as were corresponding preparations of antisera (ATS) and globulin (ATG) against the same tumors. Daily treatment with ALS or ATS inhibited growth when the carcinoma was transplanted isologously to A₅₅ mice; ALS enhanced tumor growth in A/HeJ mice. Both ALS and ATS enhanced the growth of the sarcoma. Using ^{131}I -labeled antibody, an attempt was made to calculate the number of antibody molecules/cell; the rough estimate was $1-2 \times 10^7$. The lymphocytes and tumor cells took up comparable amounts of IgG from either normal or immune serum. The mechanism of function of ALS on lymphocytes and tumor cells is discussed from the point of view of enhancing and inhibiting tumor growth.

70-624 EFFECTS OF CERTAIN CARCINOGENS ON

Periplaneta americana (L.) (E.)

Sutherland, D. J. (Rutgers State U., New Brunswick, N. J.). Nat. Cancer Inst. Monogr. 31:433-445, 1969.

Young adult or nymphal cockroaches (Periplaneta americana) were exposed to 3-methylcholanthrene, 2-fluorenamine or N,N-dimethyl-p-phenylazoaniline by several methods (in the diet, topically or by inj.), sometimes with added croton oil as an irritant. In general, less than 20% of each treated group developed abnormal growths, the sites of which were not specific for any compound. These growths were wound-healing reactions rather than malignant tumors. It is concluded that these agents are not carcinogenic to this insect.

70-625 ABNORMAL CELLULAR RESPONSES IN

Periplaneta americana (L.) RESULTING

FROM INTRACOELOMIC INJECTIONS OF BENZO[a]PYRENE.

(E.) Baerwald, R. J. (U. Wisconsin, Madison) and G. M. Boush. Nat. Cancer Inst. Monogr. 31:447-451, 1969.

Developing cockroach (Periplaneta americana) nymphs received 1 intracoelomic inj. of 3,4-benzpyrene (BP; 5 μ liter of 2 mg/ml acetone soln.). The mortality rate 1 and 2 days after BP inj. was 60-70% (attributed to acetone poisoning); the abdomens of the survivors were examined 2 weeks or more after BP admin. Abnormal cellular responses, associated with the midgut and hindgut, were seen in 10/40 by 15-28 days after BP inj. These lesions were apparently composed of non-hemocytic cells and contained an abnormal frequency of mitotic figures.

70-626 EFFECTS OF THALIDOMIDE ON Drosophila:

DEVELOPMENT AND TUMORIGENESIS. COM-

PARISON WITH POTASSIUM PHTHALATE AND SOME NON-PHTHALATE COMPOUNDS. (Fr.) Baroche, C. (Pasteur Lab., Inst. Radium, Paris). Bull. Cancer (Paris) 55(3):413-428, 1968.

When added to a standard nutrient medium fed to several strains of Drosophila, both thalidomide and potassium phthalate induced malformations in the treated insects and visible mutations in their descendants. Both agents reduced the tumor incidence among the treated insects of tumor-bearing strain cl tu, but increased the tumor incidence significantly among their descendants. Neither substance induced tumors in non-tumor-bearing strains Antibes VIII 55, cd, or w 58 i. However, a tumor incidence of 2.1% was seen in the third generation of descendants of w 58 i; and inbreeding increased this incidence to as much as 50-75% in succeeding generations. Similar admin. of toluidine blue, trypan blue, resorcinol, colchicine and aminopterin showed all of these substances to be considerably more toxic than the phthalic compounds studied.

All agents induced a significant incidence of malformations in the treated insects, but all except aminopterin (which was studied only in the original, treated larvae) failed to induce teratogenesis in subsequent generations. None inhibited tumorigenesis among treated insects of the tumor-bearing strain, while aminopterin increased it significantly. (A tendency of colchicine to inhibit it slightly was ascribed to the toxic effects of the drug, rather than to any direct action.) None exerted any effect on tumorigenesis in succeeding generations.

70-627 MALFORMATIONS AND LETHAL GROWTHS IN PLANARIA TREATED WITH CARCINOGENS.

(E.) Foster, J. A. (2199 Sharon Rd., Menlo Park, Calif.). Nat. Cancer Inst. Monogr. 31:683-691, 1969.

In adult planaria exposed to 3-methylcholanthrene (MC) or 3,4-benzpyrene (BP; 4 ml of saturated acetone soln./liter of medium; 1 24-hour exposure/week for 2 mo. before sectioning and on day 10 of forced regeneration, 9% and 7%, resp., developed lethal growths. Lethal tumors were also noted in 12/40 offspring of MC-exposed adults and in 2/75 offspring of BP-exposed adults; developmental malformations were seen in 32% and 12%, resp. When adult planaria were implanted with pellets containing paraffin and either MC or benz(a)anthracene (in a wt.:vol. ratio of 4:1) before forced regeneration, 5/10 and 4/10 regenerating animals, resp., developed lethal tumors. These tumors were apparently derived largely from neoblasts, although some metaplasia of somatic cells was considered possible.

70-628 ACTIVITY OF HETEROLOGOUS NUCLEIC ACIDS

IN THE NEWT. (It.) Camerini, E.

(Inst. Embryol. & Exper. Morphol., Milan, Italy) and T. Zavarella. Cancro 21(4):379-394, 1968.

Groups of newts (Triturus cristatus Laur.) received s.c. inj. of commercially procured substances: mammalian DNA, a phenol extract of DNA, DNA incubated with Dnase, Dnase alone, RNA, a phenol extract of RNA, RNA incubated with Rnase, Rnase alone, phosphate buffer (PBS) alone, a phenol extract of PBS, a soln. of sodium diethylaminotetraacetate, and a soln. of bentonite in PBS. The preparations were admin. to different groups of animals at 3 different seasons of the year. There was no evidence of any oncogenic activity on the part of any substance admin. However, a very high incidence of melanomas was observed among animals treated during September-October (53.6%), less incidence among those treated during January-February (34.3%), and only 4.2% tumor incidence among those treated during June-July. In no case was there any indication of a relationship between tumor incidence and the type of treatment admin., confirming that the tumors were spontaneous and their incidence controlled by thus-far unidentified seasonal or geographic factors.

70-629 MELANOTIC LESIONS OF THE EYE IN AUGUST HOODED RATS INDUCED BY URETHAN OR N-HYDROXYURETHAN GIVEN DURING THE NEONATAL PERIOD: A HISTOPATHOLOGICAL STUDY. (E.) Kendrey, G. (Med. Univ. Inst. Path., Budapest) and F. J. C. Roe. J. Nat. Cancer Inst. 43(4): 749-762, 1969.

Inbred August hooded rats were treated s.c. with urethan (U) or N-hydroxyurethan (NHU) for 8 weeks, beginning on the first day of life (1 inj./week of 1 mg/g s.c.). Melanotic lesions of 1 or both eyes were seen in 15/15 males and 11/17 females surviving 16 weeks after the beginning of U admin. In the 16-week survivors treated with NHU, 11/21 males and 11/21 females also developed melanotic lesions of 1 or both eyes. These lesions were either melanosis or melanomas, which involved the iris, ciliary body and/or choroid in different rats. The 8 melanomas of the iris were not invasive, but 2/3 choroidal melanomas showed extension through the sclera. One of the rats developed distant metastases.

0-630 BLOCKAGE OF DNA SYNTHESIS IN VIVO BY N-METHYL-N-NITROSOUREA. (Ger.) Leihues, P. (Max Planck Inst. Brain Res., Cologne, Germany). Arzneimittelforschung 19(7): 041-043, 1969.

The compound was inj. i.p. (100 and 50 mg/kg dose) into female Wistar rats (100-130 g) and the incorporation of ^3H -thymidine (0.5 mCi/kg i.v. 30 min. before death) into the DNA of several organs measured 1.5-48 hours later. Inhibition of thymidine incorporation was seen 1.5 hours after inj.; the strongest inhibition was observed after 6 hours in the spleen and intestines (3% of norm), bone marrow and kidney (3-10% of norm) and to a lesser extent in liver (5% of norm). The duration of effect also differed in different organs: after 48 hours a 5% inhibition in spleen but only 10-35% in intestines, liver and kidney was observed. Dose-dependent differences were reflected mainly in the duration of recovery phase: in the intestines the effect of 100 mg/kg and 50 mg/kg was about the same up to 3 hours after inj., but after 48 hours an inhibition of 30% with 100 mg/kg and no inhibition (values above norm) with 50 mg/kg were obtained. The compound also had a marked cytotoxic effect on proliferating cell populations. Histological examination of intestinal crypts showed some inhibition of mitosis after 15 hours, severe cytological changes after 3 hours (no mitosis, swollen and vacuolized cytoplasm, pyknosis and karyorrhectic nuclei), extensive necrosis after 6 hours and definite signs of regeneration with numerous mitotic figures after 48 hours.

7-631 ENZYME HISTOCHEMICAL STUDIES OF EXPERIMENTAL BRAIN TUMORS OF THE RAT. (Ger.) Osske, G. (Med. Acad. Erfurt Path. Inst.,

Germany), R. Warzok and W. Jänisch. Exp. Path. 3(4-5):280-289, 1969.

The occurrence and distribution of acid and alkaline phosphatase, arylesterase, leucine aminopeptidase, NADH₂ oxidoreductase, succinic dehydrogenase and cytochrome oxidase were investigated in 12 intracranial sarcomas, 7 gliomas and 3 gliosarcomas induced after latent periods of 181-337 days in 22 rats (20 Haubenratte strain E, 2 Wistar) by i.v. admin. of N-methyl-N-nitrosourea (10-25 mg/kg either twice/week, every 2 weeks, or every 4 weeks, total 29.2-67.1 mg). Strong alkaline phosphatase activity was detected in the partly enlarged blood vessel walls. While in sarcomas the activity of acid phosphatase was weak and diffusely distributed in the cytoplasm of tumor cells, it was concentrated in small cytoplasmic areas in the vicinity of nuclei in gliomas and gliosarcomas. Weak to moderate activity of arylesterase was detected in 12/22 tumors. The activity was unevenly distributed and was absent in marginal zones of necrosis. Leucine aminopeptidase was detected in only 2 tumors (1 sarcoma, 1 glioblastoma). NADH₂ oxidoreductase was present in the majority of cells of all types of tumors. Strong activity was noted in giant cells, large astrocytes, in the marginal zones of necrosis and perivascular cell accumulations. Succinic dehydrogenase was present in all tumors; a specific distribution was not observed. Weak cytochrome oxidase activity was detected in the cytoplasm of tumor cells in only one sarcoma.

70-632 CYTOPHOTOMETRIC STUDIES OF THE DNA AND HISTONE CONTENT OF EXPERIMENTALLY INDUCED TUMORS OF THE CENTRAL NERVOUS SYSTEM OF THE RAT. (Ger.) Thust, R. (Med. Acad. Erfurt Path. Inst., Germany) and W. Jänisch. Virchow. Arch. [Zellpath.] 2(2):144-153, 1969.

Studies were carried out on 6 sarcomas, 2 oligodendrogliomas and 1 glioblastoma induced by i.v. or i.p. admin. of methyl nitrosourea (MNU) in 10-25 mg/kg dose at 2-4-week intervals (latent periods were 137-243 days) or by 6,9,10-trimethyl-1,2-benzanthracene pellet implantation (latent periods were 250 days) or by transplantation of a MNU-induced intracranial sarcoma (latent periods were 33 and 41 days). The cytophotometric determinations of DNA and histones of the MNU-induced sarcomas (1 extracranial, 4 intracranial, 1 intramedullary) revealed a tendency for the development of hyperdiploid to tetraploid DNA stemlines. This high ploidy level was however reached only by the extracranial and second transplant generation of the intracranial sarcoma suggesting that the process of ploidy development in sarcomas of the central nervous system is interrupted by the premature death of the animal (caused by damage to the central nervous system). No deviation from normal values was detected in the 2 oligodendrogliomas (one of which was induced by MNU,

the other by the benzantracene compound). High level of polyploidy was detected in the giant cells of the glioblastoma multiforme. Possibly due to degenerative changes, the histone content showed no constant relationship to the corresponding DNA values.

70-633 ³H-THYMIDINE AUTORADIOGRAPHY IN EXPERIMENTALLY INDUCED TUMORS IN THE NERVOUS SYSTEM OF THE RAT. (Ger.) Citoler, P. (U. Bonn Path. Inst., Germany) and C. Thomas. Verh. Deutsch. Ges. Path. 52:380-384, 1968.

Eight neurinomas of the peripheral and cranial nerves, 2 meningeal sarcomas, 10 intracerebral and intramedullary gliomas (3/10 gliomatoses, 3/10 isomorphic and 4/10 polymorphic gliomas), and 8 adventitial cerebral sarcomas were induced in an unspecified number of Wistar-II rats by p.o. admin. of N-nitrosomethylurea (4 mg/kg/dose, 5 doses/week), following a mean induction time of 300 days. One hour prior to sacrifice, the animals received a single dose of ³H-thymidine (250 µc, i.p.). The highest labeling indices recorded in subsequent autoradiographic studies were as follows (number of tumors in parentheses): circumscribed neurinomas (2) = 2.8%, infiltrating neurinomas (6) = 6.9%, meningeal sarcomas (2, both with same value) = 5.1%, gliomatoses (3, all with same value) = 1.5%, isomorphic gliomas (3) = 8% and polymorphic gliomas (4, highly variable) = 26%. In the area immediately surrounding gliomas, neuroglial nuclei also showed increased labeling (1.2%), suggesting incipient neoplastic transformation or reactive proliferation. In 3/10 gliomas and 4/8 adventitial cerebral sarcomas, the intensity of labeling of tumor cell nuclei was approx. 10% that of the labeling of nuclei in the cells of the immediately adjoining vascular epithelium or the cells of the chorioid plexus, suggesting the functioning of a blood-brain barrier against thymidine or its metabolic products.

70-634 COMPARATIVE PATHOLOGIC AND MORPHOLOGIC STUDIES OF CEREBRAL TUMORS INDUCED TRANSPLACENTALLY AND POSTNATALLY. (Ger.) Thomas, C. (U. Bonn Path. Inst., Germany) and G. Kersting. Verh. Deutsch. Ges. Path. 52:384-388, 1968.

Of neurogenic tumors induced after latent periods of 210-460 days in 164 rats receiving long-term admin. of N-nitrosomethylurea (no additional details), 93/127 were localized in the brain, 14/127 in the spinal cord and 20/127 in the peripheral and cranial nerves. Except for a few adventitial cerebral tumors and 1 case each of meningioma and meningeal sarcoma, all intracerebral and intramedullary tumors were typical primary isomorphic gliomas, which became polymorphic and anaplastic with continued, irregular growth, and eventually ended as mixed glial-mesodermal tumors resembling gliosarcomas. In

the earlier stages, a considerable similarity with human astrocytomas, oligodendrogliomas and/or cerebral ependymomas was seen. Following a single i.v. inj. of N-nitrosoethylurea into pregnant rats (no additional details), 147 neurogenic tumors were found among 115 offspring, with a mean latent period of 250 days. These included 72 intracerebral, 26 spinal cord and 49 peripheral nervous system tumors. All were histologically clearly distinguishable from the postnatally induced neurogenic tumors. Transplacentally-induced neurinomas consisted of disseminated, spindle-cell, sarcomatous tumors tending toward cystic degeneration, with cysts whose contained fluid closely resembled blood serum in its composition. One type of transplacentally-induced tumor of the central nervous system consisted of small cells grouped in wreath- and rosette-like formations, with a characteristic macroscopic structure and cytology which did not resemble human ependymomas, neuroblastomas or medulloblastomas to the extent the postnatally-induced tumors did; the other type resembled human mixed tumors in which astrocytes and oligodendroglia were participating in simultaneous proliferation.

70-635 MORPHOLOGY AND GROWTH OF TUMORS OF THE NERVOUS SYSTEM INDUCED BY TRANSPLACENTAL ADMINISTRATION OF N-NITROSOETHYLUREA. (Ger.) Kleihues, P. (Max Planck Inst. Brain Res., Cologne, Germany), S. Matsumoto, W. Wechsler and K. J. Zülch. Verh. Deutsch. Ges. Path. 52: 372-380, 1968.

Twelve BD-IX rats received a single inj. of N-nitrosoethylurea (30-60 mg/kg, i.v., s.c. or i.p., in phosphate-buffered physiological saline) on day 13-19 of pregnancy, which induced 5 non-neurogenic and 217 malignant neurogenic tumors in 90 offspring; 137/217 tumors were localized in the brain (88%) or spinal cord (12%) and 80/217 in the peripheral nervous system (N. trigeminus = 42%, lumbosacral plexus and N. ischiadicus = 40%, plexus brachialis and intercostal nerves = 8%, N. vagus = 4%, N. acusticus = 1% and other, scattered sites = 5%). Cerebral tumors included malignant ependymomas, mixed gliomas, isomorphic oligodendrogliomas and astrocytomas. The most frequent spinal cord tumors were malignant ependymomas, with some circumscribed gliomas, isomorphic gliomas and mixed gliomas. Tumors of the peripheral nervous system included both highly and poorly differentiated, malignant neurinomas and afibrillar medulloblastomas. Autoradiographic studies of malignant ependymomas, astrocytomas and neurinomas from various tumor sites, using ³H- and ¹⁴C-thymidine, yielded relatively constant values for the duration of DNA synthesis (6-7 hours), with labeling indices ranging from 2.0%-7.5%. Considerable variations of the labeling index were seen in different sections of the same tumor, and these differences were increased markedly when ³H-thymidine was inj. every 3-4

ours for 2 days, with some sections showing a labelling index as high as 90% after a single inj. and others showing almost no increase over the original value. Mean generation times were highly variable and probably not representative, with different cell fractions within the same tumor varying markedly from the mean in both directions.

636 MORPHOLOGIC, ENZYMATIC AND HISTOCHEMICAL STUDIES OF EXPERIMENTAL PERIPHERAL NERVOUS SYSTEM TUMORS IN RATS. (Ger.) Stavrou, (U. Munich Sch. Vet. Med., Germany). Arch. Schwulstforsch. 34(4):297-308, 1969.

response to phenyldimethyltriazine (50 mg/kg/ek s.c., total 585-690 mg/animal), 4-mo.-old rague-Dawley rats of both sexes developed single or multiple cerebral and spinal cord tumors and/or infiltrating spindle cell neurinomas of the cranial and spinal nerve roots. Morphological, histological and histochemical studies of 26 of these neurinomas, with particular attention to the demonstration and distribution of hydrolase and oxidoreductase activities, appeared to confirm that they were of neuroectodermal origin.

637 TRANSPLACENTALLY-INDUCED MALIGNANT TUMORS OF THE NERVOUS SYSTEM. II. DIPHENYLNITROSOUREA IN TEN GENETICALLY-DEFINED STRAINS OF RAT. (Ger.) Druckrey, H. (Max Planck Inst. Immun. Biol., Freiburg, Germany), Landschütz and S. Ivankovic. Z. Krebsforsch. 74(4):371-376, 1970.

of 10 different inbred substrains, derived from a cross of BDI with albino Wistar rats, received a single inj. of N-nitrosoethylurea (50 mg/kg, i.v. in aqueous soln. into a tail vein) on day 15 of pregnancy. A total of 238 malignant neurogenic tumors resulted in 162/179 offspring, although only 12/179 developed non-neurogenic tumors (3/12 ovarian carcinomas, 2/12 fibroblastomas, 2/12 unspecified uterine tumors, 1/12, each, an unclassified tumor of the adrenal cortex, s.c. fibrosarcoma, stem cell leukemia, disseminated reticulosis with an unspecified tumor of the spleen, and pituitary adenoma). Cerebral tumors included gliomas (chiefly oligodendrogliomas), ependymomas, astrocytomas and mixed malignant tumors. Tumors of the peripheral and cranial nerves were all malignant neurinomas. The substrains showed considerable differences with respect to mean induction times, total number of neurogenic tumors, and their distribution in terms of utilization. These differences, in turn, were observed to be substrain-specific.

638 MORPHOLOGY OF TUMORS INDUCED BY N-NITROSO COMPOUNDS IN THE UPPER DIGESTIVE TRACT OF RATS. (Ger.) Thomas, C. (U.

Freiburg i. Br. Path. Inst., Germany) and B. T. So. Arzneimittelforschung 19(7):1077-1081, 1969.

Based on macroscopic and histologic findings of 618 preneoplastic changes and 506 carcinomas induced in rats by 25 different N-nitroso compounds (by several routes of admin. and in different doses), tumor development in the upper g.i. tract (mouth to forestomach) was divided into 3 stages: non-neoplastic early changes; mucous membrane regeneration and preneoplastic changes; and tumor formation (papillomas and carcinomas). Each stage is briefly described. It is concluded that these tumors develop from hyperplasia of the squamous cell epithelium ("umbilicated lesions" or basal cell hyperplasia). Experimental animal tumors in their early stages resemble human carcinomas *in situ*; the histologic structures of human and animal tumors are comparable except that exophytic growth predominates in the human tumors.

70-639 BACTERIAL REDUCTION OF NITRATE IN THE HUMAN STOMACH AS A CAUSE FOR NITROSAMINE FORMATION. (Ger.) Sander, J. (U. Tübingen Inst. Hyg., Germany) and F. Seif. Arzneimittelforschung 19(7):1091-1093, 1969.

Gastric contents from 31 pts. (fasting and that obtained at 10-min. intervals for 50 min. after admin. of a drink containing 100 mg sodium bicarbonate, 300 mg sodium nitrate, 1000 mg glucose and 10 mg diphenylamine) were examined for the presence of nitrite and nitrosamine. Nitrite was present in fasting gastric content in 8/31 and was formed after admin. of the drink in all whose initial (fasting) pH was above 4. It was present in 1 μ Mol - 4 μ Mol quantities when the pH remained above 5 for at least 30 min. With lowering of pH the amount of nitrite was reduced. In some pts. nitrite was present even at pH 1.5 but only in the mucous areas in which nitrate-reducing bacteria are protected from the effect of gastric acid. Nitrite formed in the stomach enabled the synthesis of diphenylnitrosamine from diphenylamine. The best conditions for this synthesis existed when the pH decreased gradually after admin. of the drink. Nitrosamine amounts of 2-10 μ g were detected in 11/31 pts. who showed strong nitrite formation and a gradual decrease of pH to a value of 3. In 5 pts. in whom the buffering capacity of the drink did not counteract stomach acidity, nitrosamine amounts of less than 1 μ g were detected.

70-640 STUDY OF THE BIOLOGICAL ACTIVITY OF 3,4-BENZOPYRENE - II. METABOLISM OF VARIOUS POLYCYCLIC HYDROCARBONS BY HEPATIC ENZYMES BEFORE AND AFTER INDUCTION BY 3,4-BENZOPYRENE. (Fr.) Rondia, D. (U. Liege Toxicol. Lab., Belgium) and P. Delwaide. Biochem. Pharmacol. 18(6):1269-1274, 1969.

Supernatants of pools of rat liver homogenates representing 10 livers each were used to study the *in vitro* metabolism of 18 polycyclic hydrocarbons: fluorene, anthracene, phenanthrene, pyrene, fluoranthene, naphthacene, benzanthracene, 3,4-benzpyrene (BP), benz(e)pyrene, perylene, benz(b)fluoranthene, anthanthrene, dibenz(a,h)-anthracene, benz(g,h,i)perylene, dibenz(a,c)-anthracene, coronene, dibenz(d,e,f,p)chrysene, and benz(a)naphtho(c,d,e)naphthacene. The homogenates were derived from untreated rats of an unspecified strain and from rats treated with unspecified doses of BP, 24 hours before sacrifice. All of the compounds were metabolized by supernatants of normal rat livers at a rate which varied from substrate to substrate and bore no apparent relationship to molecular wt. Except in the case of dibenz(a,c)anthracene and coronene, the rate of metabolism was increased when the compounds were incubated with supernatants of the livers from BP-treated animals, again without apparent relationship to molecular wt. and without discernible relationship to either the control metabolic rates or the chemical characteristics of the substrates. The speed of metabolism of the carcinogenic polycyclic hydrocarbons which were studied did not differ significantly from that of the non-carcinogenic compounds.

70-641 BIOLOGICAL ACTIVITY OF 3,4-BENZPYRENE - III. LOCALIZATION OF TRIATED 3,4-BENZPYRENE IN THE RAT FOLLOWING INTRAPERITONEAL ADMINISTRATION. (Fr.) Delwaide, P. A. (U. Liege, Belgium). Biochem. Pharmacol. 18(6): 1275-1283, 1969.

The distribution of a tracer dose of ^3H -3,4-benzpyrene (BP) was studied in tissue homogenates of the liver, kidney, adrenals, spleen, testis, and heart, at intervals of 30 min.-24 hours after i.p. admin. to immature male albino rats, with measurements made of both total radioactivity and the radioactivity of a petroleum ether extract of each of these homogenates. Both types of measurement were also made in the soluble, microsomal, nuclear, and mitochondrial fractions of the liver cells. As indicated by measurements of total radioactivity, somewhat greater amounts of the tracer were found in the liver, spleen, and kidney, reaching a max. within 4 hours and then decreasing slowly, with radioactivity still demonstrable after 24 hours. The conc. in the adrenals and heart was also max. at 4 hours. It was max. in the testis at 6 hours. No clear-cut organ specificity could be demonstrated, although a temporary loading in the spleen was demonstrable at 1 hour (only) in animals receiving a larger dose of BP (20 mg/kg, i.p.) at the same time as the tracer dose. Following the tracer dose, radioactivity in the petroleum ether extracts decreased progressively throughout the 24-hour observation period, without reaching zero in any case. This phenomenon was intensified in animals receiving the

treatment dose. Following the tracer dose, radioactivity in the soluble fraction of the liver cells increased progressively and significantly, paralleled by a decrease in the microsomal fraction. In contrast, the treatment dose markedly increased the radioactivity of the microsomal fraction, at the expense of the soluble fraction. No clear-cut specificity could be demonstrated as concerned any hepatic cellular fraction, with respect to level of activity or speed of fixation. The phenomena observed may be explained as results of the hydroxylation process, and that most of the BP admin. was involved in nonspecific processes of fixation and metabolism.

70-642 CHARACTERISTICS OF NITRO REDUCTION OF THE CARCINOGENIC AGENT, 4-NITROQUINOLINE N-OXIDE. (E.) Kato, R. (Nat. Inst. Hyg. Sci., Tokyo), A. Takahashi and T. Oshima. Biochem. Pharmacol. 19(1):45-55, 1970.

The reduction of 4-nitroquinoline N-oxide (4-NQO) by rat liver was compared to that of the non-carcinogen p-nitrobenzoic acid (p-NBA). The NADPH-dependent reduction of 4-NQO was performed predominantly by the supernatant of liver microsomes, while p-NBA was reduced mainly by microsomes. Large amounts of the reduction product 4-hydroxyaminoquinoline N-oxide (4-HAQO) from 4-NQO rapidly accumulated in the incubation mixture, in contrast to small amounts of p-hydroxyaminobenzoic acid (p-HABA) from p-NBA. Flavin mononucleotide, and admin. of phenobarbital and methylcholanthrene, stimulated p-NBA reduction, but not 4-NQO reduction. Dicumarol ($1 \times 10^{-4}\text{M}$) inhibited 4-NQO reduction in supernatant by 94% and p-NBA reduction by 29%. Reduction of 4-NQO to 4-HAQO seems attributable mainly to DT diaphorase, while hydroxyamino derivatives of other nitro compounds are slowly reduced by nitro reductase, and that the accumulation of 4-HAQO is responsible for 4-NQO carcinogenesis.

70-643 IN VITRO BREAKDOWN OF 3,4-BENZPYRENE BY RAT LIVER MICROSOMAL ENZYMES AND ITS DEPENDENCE ON THE AGE AND SEX OF THE EXPERIMENTAL ANIMALS. (Ger.) Dehnen, W. (U. Dusseldorf Med. Inst. Air Hyg., Germany), R. Tomingas and H. Schaghali. Z. Krebsforsch. 73(4):363-370, 1970.

Male and female Wistar rats of varying ages received a single inj. of 3,4-benzpyrene (BP = 1 mg/100 g, i.p. in tricaprylin), 24 hours prior to sacrifice. Incubation of the microsomal fraction of the liver homogenate with BP, and paper chromatographic and spectrophotometric determination of the resulting BP content was used as an index of liver microsomal enzyme induction. Although the capacity for such induction remained demonstrable throughout the life of the pretreated animals (in contrast to untreated controls, in which enzyme activity was

no longer demonstrable after 18 mo. of life), it showed extreme individual variations and remained at a max. only through day 20, declining progressively thereafter but never quite reaching zero. In the treated animals, hydroxylase activity also decreased, slowly but progressively, after day 50.

70-644 ENZYMATIC TRANSFORMATION OF CARCINOGENIC NITROSAMINES. (Ger.) Neunhoeffer, O. (U. Saarland Inst. Org. Chem., Germany), G. Wilhelm and G. Lehmann. Z. Naturforsch. [B] 5(3):302-307, 1970.

Incubation of rat liver and kidney homogenates with dimethyl-, diethyl-, di-n-propyl- and N-examethyleneiminonitrosamine confirmed by thin-layer chromatography that the nitrosamine compounds were first transformed into their corresponding amidoximes and then hydrolyzed to yield primary amines and hydroxamic acids, with the eventual separation of hydroxylamines in response to slow, continued, spontaneous hydrolysis. The yield of the products of such transformation increased directly as the degree of carcinogenicity of the nitrosamine compounds employed. In quantitative assays, the total recovery of a nitrosamine compound and its metabolic products was invariably well within the limits of the margin of error established for the original dosage, appearing to confirm that interference from other metabolic processes is highly unlikely. Both cyanide and sulfite increased the activity of the enzyme system significantly, suggesting that sulfhydryl enzymes took part in the metabolic process, probably in the form of disulfides, which began to build up after the first 6 hours of incubation. The enzymatic process was entirely suppressed by the presence of thymidine, possibly due to inactivation of such sulfhydryl enzymes by opening of the thiazole ring and the resulting formation of oxidized disulfides.

70-645 SUBFRACTIONATION OF RAT LIVER MICROSOMES: EFFECTS OF PHENOBARBITAL AND METHYLCHOLANTHRENE. (E.) Murphy, P. J. (Eli Lilly Co., Indianapolis, Ind.), R. M. Van Frank and T. L. Williams. Biochem. Biophys. Res. Commun. 37(4):697-704, 1969.

Rats pretreated with 5 mg/kg/day of phenobarbital (PB) for 5 days, their livers homogenized, and the 10,000 x g supernatant subjected to rate-zonal centrifugation, the distribution of cytochrome P-450 showed an increase in the lighter portion of the gradient, corresponding to the smooth endoplasmic reticulum, whereas in rats pretreated with 3-methylcholanthrene (MC), there was a marked increase in the P-450 content of the particles having higher S values. These distributions were distinct even when MC and PB were administered simultaneously, suggesting that the P-450 is formed in, or bound to different

vesicles. The distribution induced by MC is inhibited by ethionine (100 mg/kg 60 and 30 min. prior to MC) and thioacetamide (50 mg/kg/day for 5 days).

70-646 THE ROLE OF HEME SYNTHESIS DURING THE INDUCTION OF HEPATIC MICROSOMAL CYTOCHROME P-450 AND DRUG METABOLISM PRODUCED BY BENZOPYRENE. (E.) Baron, J. (U. Michigan Med. Sch., Ann Arbor) and T. R. Tephly. Biochem. Biophys. Res. Commun. 36(4):526-532, 1969.

Male Holtzman rats (130-170 g), inj. i.p. with 20 mg/kg benzpyrene (BP) in corn oil showed (1) a 32% stimulation of glycine-2-¹⁴C incorporation into hepatic microsomal heme *in vivo*, which was inhibited by 3 g/kg of 3-amino-1,2,4-triazole (AT) i.p. in saline and an increase in delta-aminolevulinic acid (ALA) synthetase within 24 hour. This was not affected by AT, but was prevented by actinomycin D (3 mg/kg), (2) stimulation of cytochrome P-450 synthesis and N-demethylation of 3-methyl-4-monomethylaminoazobenzene. This was antagonized by AT, (3) no change in the hepatic microsomal level of cytochrome b5 or NADPH cytochrome c reductase activity. It is thought that BP stimulates heme synthesis by enhancing ALA synthetase, which leads to an increased synthesis of cytochrome P-450 and certain microsomal oxidations.

70-647 CHANGES IN ARYL HYDROCARBON HYDROXYLASE ACTIVITY AND MICROSOMAL P₄₅₀ DURING POLYCYCLIC HYDROCARBON TREATMENT OF MAMMALIAN CELLS IN CULTURE. (E.) Nebert, D. W. (NIH, Bethesda, Md.). Biochem. Biophys. Res. Commun. 36(6):885-890, 1969.

Cultures derived from 10-14-day-old hamster fetuses were treated with 13 μM benzanthrane (BA). After 21 hour exposure to BA, the activity of aryl hydrocarbon hydroxylase increased more than 20-fold while the microsomal P₄₅₀ content increased less than double. A blue spectral shift in the P₄₅₀-CO absorption max. was detectable after 8 hour; by 21 hour, the only visible peak was at 446 nanometers (nm). When the cells were regrown in fresh medium, the hydroxylase activity and the microsomal P₄₅₀ content were greatly reduced and the 450 nm peak was again visible. The blue spectral shift was observed in the presence of increased hydroxylase activity and in the absence of BA, but not when BA was present along with a substance blocking protein synthesis.

70-648 OXIDATION OF CARCINOGENIC AZO-DYES. VII. METABOLITES OF SOME 4'-SUBSTITUTED DERIVATIVES OF DIMETHYLAMINOAZOBENZENE IN THE BILE OF RATS. (E.) Marhold, J. (Res. Inst. Org. Synth., Pardubice-Rybitvi, Czechoslovakia), V. Rambousek, J. Připalová and M. Matrká. Neoplasma (Bratisl.) 16(2):191-194, 1969.

After p.o. admin., 9 derivatives of dimethylaminobenzene, substituted at position 4', were excreted in the bile of rats in N-demethylated form, and in some derivatives the N-demethylated substituent was replaced by hydroxyl. The carcinogenic activities of the azo-dyes corresponded to metabolic hydroxylation rather than N-demethylation.

70-649 IN VIVO OXIDATION OF GLUCOSE-1-¹⁴C AND GLUCOSE-6-¹⁴C IN MICE WITH 7,12-DIMETHYLBENZ[a]ANTHRACENE-INDUCED TUMORS. (E.) Burki, H. R. (Northwestern U. Med. Sch., Chicago, Ill.) and G. T. Okita. J. Nat. Cancer Inst. 43(3):643-651, 1969.

Virgin female C57BL/6J mice were admin. a single i.v. inj. of 7,12-dimethylbenzanthracene (DMBA; 0.75 mg) and 34 weeks after glucose-¹⁴C oxidation was measured. In those developing ovarian tumors, there was a reduced rate of D-glucose-6-¹⁴C (G-6-¹⁴C) oxidation compared to controls, no significant change in D-glucose-1-¹⁴C (G-1-¹⁴C) oxidation, a higher blood glucose level, increased incidence of estrus, and an increased ratio of G-1-¹⁴C/G-6-¹⁴C oxidation. In further studies, 40-70 mg of mammary tumor from 10-mo.-old C57BL mice were bathed 20 min. in a fat emulsion or in 5 mg/ml DMBA, then inj. into untreated virgin, female mice and mice treated 16 days prior with 0.75 mg DMBA i.v., and again, 5 days prior, with 0.5 mg i.p. There was a decreased G-6-¹⁴C oxidation only in those mice developing tumors (fibrosarcomas) who were pretreated with DMBA, suggesting that this agent directly influences glucose metabolism in tumor-bearing mice.

70-650 RECIPROCAL INFLUENCE OF 7,12-DIMETHYLBENZ(a)ANTHRACENE (DMBA) AND PARA-DIMETHYLAMINOAZOBENZENE (DAB), ADMINISTERED TO RATS SIMULTANEOUSLY. (Fr.) Lacassagne, A. (Inst. Radium, Paris) and L. Hurst. Bull. Cancer (Paris) 56(2):169-176, 1969.

One group of male Wistar rats received a diet deficient in protein and riboflavin, containing 7,12-dimethylbenzanthracene (DMBA, 10 mg/kg for 48-369 days). Another group received the same deficient, DMBA-containing diet, with the addition of p-dimethylaminoazobenzene (DAB = 600 mg/kg for 24-350 days). In the group treated with DMBA alone, there was no loss of body wt. during the first 10 mo. of treatment and no liver tumors, although adrenal wt. was increased, with lipid degeneration of the spongocytes in some cortical areas and much lipofuscin demonstrable in reticulated tissue, despite the absence of adrenal necrosis and hemorrhage. In the second group, although DMBA failed to inhibit the hepatic carcinogenic activity of DAB, with multiple, voluminous hepatic tumors demonstrable by day 234, DAB appeared to afford complete protection against the effects of DMBA on the

adrenals. DMBA also failed to inhibit the toxicity of DAB. Loss of body wt. was immediate and progressive, reaching one-third the initial wt. within 8 mo. One animal in each group developed a large, unilateral, renal tumor, ascribed to the action of DMBA. Neither group showed significant effects on testicular structure, that of the testicular adnexae, or spermatogenesis, except for the longest survivor treated with DMBA alone, which developed testicular atrophy and gross loss of body wt. in the presence of an ascitic, renal cortical adenoma. The renal tumor in the animal treated with both substances was an epithelial neoplasm with considerable infiltration by malignant, polymorphous, mesenchymal elements, giving the overall appearance of a rhabdomyosarcoma.

70-651 MICROELECTROPHORESIS IN AGAROSE GEL OF SOLUBLE RAT LIVER PROTEINS DURING AMINOAZO DYE CARCINOGENESIS. (E.) Louis, C. J. (U. Melbourne, Australia) and J. M. Blunck. Oncologia (Basel) 23(4):257-264, 1969.

A microelectrophoretic method using agarose gel supported on microscope slides is described. In soluble, cytoplasmic proteins of livers from adult, male Sprague-Dawley rats receiving food with 0.06% 3'-methyl-4-dimethylaminoazobenzene (3'-MeDAB, up to 12 week), this method, along with autoradiography using tritiated 3'-MeDAB, revealed a slight increase in the dye-binding proteins of bands A and B after 2 week, followed by a decrease detectable at 4 weeks. Bands A and B were markedly diminished in hepatoma tissue but normal in surrounding histologically normal liver tissue.

70-652 ACTIVATION OF GLUTATHIONASE IN RAT LIVER DURING CARCINOGENESIS. (E.) Fiala, S. (U. Southern California, Los Angeles) and A. E. Fiala. Naturwissenschaften 56(11):565, 1969.

The activation of glutathionase was detected in the microsomal fraction of rat liver after 8 days of feeding with 3'-methyl-4-dimethylaminoazobenzene (3'-MeDAB). The enzyme almost disappeared after withdrawal (49 days) of 3'-MeDAB, and reappeared in much higher activity in the induced hepatoma. An increase was also seen in the transplanted Novikoff or Morris hepatomas, but not in adrenalectomized or hypophysectomized rats fed 3'-MeDAB, which usually did not develop hepatomas, and not in regenerating liver or hepatoma-bearing rats.

70-653 HEPATOCARCINOGENESIS IN MICE WITH THE SIMULTANEOUS ADMINISTRATION OF DIETHYLNITROSAMINE AND THE VIRUS MOTOL. (E.) Kordač, V. (Inst. Med. Microbiol., Prague), E. Schön and A. Braun. Neoplasma (Bratisl.) 16(5):485-490, 1969.

Motol virus (isolated from sera of pts. with infectious hepatitis; i.p., 0.1 LD₅₀) and diethylnitrosamine (DENA; p.o., 0.009 g/kg/day) acted synergistically in increasing the ratio of liver wt./body wt. and in inducing hepatocarcinomas in white mice (18-20 g). Motol virus alone, DENA alone, and the combination (admin. simultaneously) induced hepatocarcinomas in 0/17, 1/17, and 15/15 mice, resp., surviving 21 week after the beginning of treatment.

70-654 TRANSPLANTABLE HEPATOMAS INDUCED IN STRAIN-2 GUINEA PIGS BY DIETHYLNITROSAMINE: CHARACTERIZATION BY HISTOLOGY, GROWTH, AND CHROMOSOMES. (E.) Zbar, B. (NCI, Bethesda, Md.), H. T. Wepsic, H. J. Rapp, J. Whang-Peng and T. Borsos. J. Nat. Cancer Inst. 33(4):821-831, 1969.

Hepatomas were induced in 6 strain-2 guinea pigs by feeding diethylnitrosamine (0.042 g/liter water for 7-11 mo.). All 6 primary tumors, consisting of mixtures of hepatocellular and adenocarcinoma cell types, were isologously transplantable by i.m. inj. of 10⁶-10⁷ primary cells; 4/6 primary tumors (lines 1, 4, 7 and 8) were transplantable by i.p. inoc. Histologically, transplant lines 2, 4, 5 and 7 differed from each other and from lines 1 and 8, which were alike. Lines 1 and 7 were also transplantable by intradermal inj., and a subline 7B, differing from line 7 in histology, transplantability and chromosomal constitution, was developed by intradermal inj. of line 7 ascites cells. On chromosomal analysis, lines 4 and 7 differed from each other and from lines 1, 7B, and 8, which were alike.

70-655 ANTIGENIC SPECIFICITY OF HEPATOMAS INDUCED IN STRAIN-2 GUINEA PIGS BY DIETHYLNITROSAMINE. (E.) Zbar, B. (NCI, Bethesda, Md.), H. T. Wepsic, H. J. Rapp, T. Borsos, B. S. Kronman and W. H. Churchill, Jr. J. Nat. Cancer Inst. 43(4):833-841, 1969.

Guinea pigs were immunized intradermally or i.m. with tumor cells from 6 transplantable hepatomas induced by diethylnitrosamine in strain-2 guinea pigs. Subsequent testing for delayed cutaneous hypersensitivity revealed antigenicity in 5 of the 6 hepatomas; 2 of the 5 antigenic tumor lines (lines 1 and 8) shared a common antigen, and the remaining 3 were antigenically specific. After a number of transplant generations, 2 of the 3 antigenically specific-tumor lines developed antigens common to tumor line 1. A transplantable, virus-induced, strain-2 guinea pig leukemia did not cross-react with hepatoma line 1 in delayed cutaneous hypersensitivity.

70-656 TUMOR-SPECIFIC ANTIGENS: DETECTION BY LOCAL TRANSFER OF DELAYED SKIN HYPERSENSITIVITY. (E.) Kronman, B. S. (NCI, Bethesda,

Md.), H. J. Rapp and T. Borsos. J. Nat. Cancer Inst. 43(4):869-875, 1969.

Delayed hypersensitivity to diethylnitrosamine-induced hepatomas in strain-2 guinea pigs was passively transferred to isologous skin by intradermal inj. of peritoneal exudate cells (PE) from immunized guinea pigs. The extent of the passive skin reaction depended on the ratio and absolute amounts of tumor cells and PE, and on the time between immunization and harvesting of donor PE. Passive skin reactions were usually correlated with suppression of tumor growth. The antigenic specificity of 5 hepatoma cell lines was the same in passive and in active delayed cutaneous hypersensitivity.

70-657 SOLUBLE TUMOR-SPECIFIC TRANSPLANTATION ANTIGENS FROM METHYLCHOLANTHRENE-INDUCED GUINEA PIG SARCOMAS. (E.) Holmes, E. C. (NCI, Bethesda, Md.), B. D. Kahan and D. L. Morton. Cancer 25(2):373-379, 1970.

Two histologically different methylcholanthrene-induced sarcomas from strain 2 guinea pigs were treated with low intensity ultrasound to liberate soluble tissue antigens. The immunization of syngeneic hosts either with the antigen preparation or with temporary tumor growth conferred tumor-specific resistance to s.c. transplantation of tumor.

70-658 FURTHER EVIDENCE OF COMMON ANTIGENIC PROPERTIES IN CHEMICALLY INDUCED SARCOMAS OF MICE. (E.) Reiner, J. (Sloan-Kettering Inst. Cancer Res., New York, N. Y.) and C. M. Southam. Cancer Res. 29(10):1814-1820, 1969.

Tumor-specific resistance to isologous transplants (s.c.) of methylcholanthrene-induced sarcomas developed in 6-14-week-old C57BL/6 mice, each immunized with tumor cells from one of 5 tumors, except for one tumor which could not be evaluated because of low transplantability. Immunization with up to 4 tumors, sequentially or simultaneously, in some combinations induced cross-resistance to subsequent transplant challenge with a tumor not included in the immunizations. Similar results were obtained when x-irradiated cells were used for immunization, except that resistance of the tumor was significantly decreased by immunization with the x-irradiated cells of the other 4 tumors.

70-659 CHEMICAL CARCINOGENESIS AND ITS DEPENDENCE ON THE HOST. (It.) Yoshida, T. (Jap. Found. Cancer Inst., Tokyo). Gazz. Sanit. 40(3):106-108, 1969.

Rats of unspecified strain and age received unspecified doses of dimethylaminoazobenzene (DAB) for 2 mo. (route not specified), an

interval which was insufficient to induce hepatomas, although longer treatment with DAB had induced hepatomas in 100% of treated animals. During the 3 mo. following, they received unspecified doses of o-aminobenzene (AB; route not specified), which is not a carcinogen. At the end of 7 additional mo., only 7/30 were surviving, with hepatomas demonstrable in 2/7. In another group, when the order of admin. of DAB and AB was reversed, none of the animals developed malignancy. In a correlative experiment, 2 groups of rats received unspecified doses of 3-methylcholanthrene (MC) for 4 and 5 mo., resp., by topical (dorsal) application. No sign of malignancy was found during the next 7-8 mo. although MC admin. topically for a longer period had induced s.c. sarcomas in an unspecified percentage of treated animals. The animals then received unspecified doses of dimethylaminostilbene (DAS), p.o. for 5 mo. At the end of an additional 3 mo. observation period, only 8/32 animals were surviving; 8/8 showed keratoblastic squamous cell carcinomas at the site of MC application (although DAS alone induced similar carcinomas only in the auditory canals of 91% of rats treated for longer periods of time). Among animals treated in the same way, but receiving MC for only 1-3 mo., 14/36 were surviving at the end of 20 mo.; skin carcinomas were demonstrable in 7/14, hepatomas in 4/14, carcinomas of the auditory canal in 2/14, and no tumors in 1/14. It is concluded that either a noncarcinogen or a very weak carcinogen could induce tumors in animals in which a predisposition to tumor had been created by the prior admin. of a carcinogenic agent in a total dose which was insufficient to induce tumor by itself.

70-660 ORGAN SPECIFIC EFFECT OF THIOACETAMIDE ON LIVER GLYCOGEN. (E.) Sapre, N. N. (Tata Mem. Ctr., Bombay, India), S. V. Gothoskar and S. V. Bhide. Indian J. Exp. Biol. 7(1): 4-7, 1969.

In the livers of male Swiss mice treated 24 hour previously with thioacetamide (250 mg/kg i.p.), significant reductions of glycogen, protein, glucose-6-phosphatase, fructose-1,6-diphosphatase and phosphoglucomutase levels were seen. Total DNA and RNA contents remained unchanged in the liver and kidney. Kidney and muscle glycogen levels were also unchanged. It is suggested that thioacetamide inhibits glycogen biosynthesis in the liver.

70-661 INFLUENCE OF REFRIGERATION ON AFLATOXIN PRODUCTION BY STRAINS OF Aspergillus flavus. (E.) van Walbeek, W. (Food Drug Directorate, Ottawa, Canada), T. Clademenos and F. S. Thatcher. Canad. J. Microbiol. 15(6): 629-632, 1969.

Five strains of Aspergillus flavus produced aflatoxin in broth and/or agar for up to 4 weeks during refrigeration at 7°C or 10°C. The 2 most

active strains at room temperature, 381 Fr and V3734/10, were also the most active toxin producers during refrigeration. Toxin production during refrigeration was markedly increased by preincubation at room temperature for 24 hr. and was greater on solid than liquid media. The hazard of toxin production in refrigerated foods is discussed.

70-662 TRANSFORMATION OF AFLATOXIN B₁ BY STEROID-HYDROXYLATING FUNGI. (E)

Detroy, R. W. (Northern Reg. Res. Lab., Peoria, Ill.) and C. W. Hesseltine. Canad. J. Microbiol. 15(6):495-500, 1969.

In fungal cultures, aflatoxin B₁ was transformed to a new fluorescent-blue compound (designated R₀) by 6/17 fungi, particularly Dactylium dendroides, Absidia repens, and Mucor griseocyanus. Washed mycelia of D. dendroides in 0.02 M phosphate buffer catalyzed a 25-30% conversion of aflatoxin B₁ in 20 hour. The fluorescent compound was distinguished from aflatoxin B₁ by thin-layer chromatography on silica gel (R_f 0.57), separated by column chromatography, and studied by spectrophotometry. R₀ yielded UV spectral peaks at 325 mμ, 261 mμ and 254 mμ; acidification did not alter the UV spectrum, suggesting an intact lactone ring. Infrared absorption peaks at 1760 cm⁻¹ and 1685 cm⁻¹ indicated a functional change in ring carbonyls; a broad band at 3400 cm⁻¹ suggested hydroxylation. The fungal systems also converted aflatoxin B₁ to another blue fluorescent compound (R₁) distinguished by its R_f of 0.50 in thin-layer chromatography.

70-663 EXTRACTION OF AFLATOXINS. (Ger.)

Bösenberg, H. (U. Munster Inst. Hyg., Germany) and G. Gerke. Arch. Hyg. Bakt. 153(1): 33-36, 1969.

Preparation and purification of aflatoxins is described. It involves extraction of the toxins from cultures of Aspergillus flavus with chloroform, precipitation of impurities with methanol and separation by thin-layer chromatography after pre-development with diethylether or petroleum ether and main development with a chloroform-methanol mixture in a 97:3 ratio. A chromatographically and UV spectrophotometrically pure aflatoxin is obtained. Amounts can then easily be calculated by using the molar extinction coefficient reported in the literature.

70-664 OCCURRENCE OF FLUORESCENT DERIVATIVES OF AFLATOXIN. (Ger.) Bösenberg, H. (U. Munster Inst. Hyg., Germany). Arch. Hyg. Bakt. 153(1):37-40, 1969.

Derivatives of aflatoxin were obtained by UV irradiation of aflatoxin B₁ or i.v. inj. of 500 μg of aflatoxin B₁ or G₁ into 100-120 g Wistar BR 46 rats and extraction of organs and excretions

, 8, 24 and 96 hour later. These substances could not be differentiated from the original Flatoxin by thin-layer chromatography alone (using several of the recommended solvents); however, they showed different UV absorption spectra. UV absorption spectrophotometry is therefore strongly recommended, in addition to thin-layer chromatography, for the detection of different aflatoxin derivatives.

665 PATHOLOGY OF THE BILIARY CANALICULI IN THE TROUT. (Fr.) Codegone, M. L. Turin Inst. Anat., Italy), A. Provana and Ghittino. Rev. Path. Comp. 68(5-6):349-354, 1968.

Cholangitis was demonstrable in 82% of rainbow trout fed a diet of fresh beef liver containing *Cereculia foetida* (S = 500 ppm, containing 55% cyclopropanes), 59.6% of those fed pellets of cotton-oil cake containing aflatoxin (A), 40.5% of those fed pellets of cotton-oil cake free of aflatoxin (F), and 44.6% of those fed a flour derived from aflatoxin-free cotton-oil cake and mixed with a conventional synthetic diet (M). The frequency of incidence was only 27% for control fish fed the synthetic diet alone; ranged from 32.5% - 38% in fish which were fed fresh beef liver alone, liver + M, liver + "Gossypol" or liver + "CMC". Of the fish developing cholangitis in the presence of S, A, F and M, 73%, proliferation of oval cells was seen in 77%, 87.9%, 58.0% and 55.6%, resp., (as compared to 63.0% in the presence of "Gossypol", 17% for the control diet, and a range of 16-31.7% for the other experimental diets). Comparable tabulations for fish developing new canaliculi (following thickening of the external walls of the existing, cholangitic canaliculi, without narrowing or other apparent change of the lumina) were 7.3%, 9.2%, 1.6% and 0.3%, resp., compared to none for the control and other experimental diets. Only fish receiving aflatoxin developed cholangiomas (2.2% of those which developed cholangitis in the presence of aflatoxin compound).

666 AFLATOXICOSIS IN COHO SALMON. (E.) Halver, J. E. (Western Fish Nutr. Lab., Seattle, Wash.), L. M. Ashley and R. R. Smith. Nat. Cancer Inst. Monogr. 31:141-150, 1969.

Young coho salmon (*Oncorhynchus kisutch*), 50 days of force-feeding with aflatoxin B₁ (5-15 mg/kg/day) induced toxic liver damage in 10 days when the fish were held in 15° C water, but only the higher doses of AB (8-10 mg/kg/day over at least 5 days) induced acute, fatal hemorrhagic necrosis of the liver. In rainbow trout (*Salmo gairdnerii*), a 5-day course of AB at a lower dose (0.5 mg/kg/day) induced fatal hemorrhagic liver necrosis in all fish by day 11. Chronic feeding with AB (20 µg/kg dry diet/day for 20 mo.; 15° C water) did not induce hepatomas

in *O. kisutch*, but all surviving trout developed typical hepatomas. The coho salmon is 10-30 times more resistant to aflatoxicosis than the rainbow trout, and generally refractory to hepatoma induction by chronic AB feeding.

70-667 INVESTIGATIONS OF THE NATURE OF THE BINDING OF AFLATOXIN B₁ WITH DNA. (E.) Clifford, J. I. (Univ. Coll. Hosp. Med. Sch., London) and K. R. Rees. Biochem. Pharmacol. 18(12):2783-2785, 1969.

Varying amounts and proportions of calf thymus DNA and aflatoxin B₁ (AB) were mixed in solution and ultracentrifuged to produce a pellet, in which the amounts of DNA and AB were measured by spectrophotometry of the supernatant. With a constant amount of DNA (2.8 mg) and varying amounts of AB, an approx. constant percentage (20-30%) of AB was precipitated with the entire 2.8 mg of DNA, suggesting a relatively weak, noncovalent binding of DNA and AB. Difference spectra of the mixtures consisted of continuous curves, indicating no stoichiometry in the reaction. Mixtures of nucleosides and AB yielded difference spectra similar to those of DNA and AB.

70-668 THE METABOLISM OF AFLATOXIN B₁ IN RATS. (E.) Purchase, I. F. H. (Nat. Nutr. Res. Inst. Council Sci. Indust. Res., Pretoria, South Africa) and M. Steyn. Brit. J. Cancer 23(4):800-805, 1969.

At 0.5-8.0 hour after p.o. admin. of aflatoxin B₁ (10 mg/kg) in dimethyl sulfoxide (10 mg/ml) to Wistar rats, males and females did not differ in their rate of gastric absorption of aflatoxin B₁, but the amounts of the metabolite aflatoxin M₁ in the kidney, liver, and intestine were higher in females than in males, suggesting that females metabolize aflatoxin B₁ more rapidly than males.

70-669 CUTANEOUS LESIONS PRODUCED BY TOPICAL APPLICATION OF AFLATOXIN TO RABBIT SKIN. (E.) Joffe, A. Z. (Hebrew U. Hadassah Med. Sch., Jerusalem, Israel) and H. Ungar. J. Invest. Derm. 52(6):504-507, 1969.

Characteristic epidermal lesions were seen in the depilated skin of rabbits after applications of aflatoxins in chloroform solution. A mixture of aflatoxins B₁ and B₂ caused intraepidermal vesicles at low concentration, and epidermal bullae at an intermediate concentration, and epidermal necrosis at high concentration. A preparation of aflatoxin G₁ had about the same toxic effects as the aflatoxin B mixture at similar doses. It is suggested that persons handling peanuts or other grain contaminated with aflatoxin-producing *Aspergillus flavus* may develop occupational dermatoses.

70-670 EFFECT OF AFLATOXINS ON RAT LIVER LYSOSOMES. (E.) Balasubramaniam, K. (U. Ceylon, Peradeniya), S. Wijesundera, S. N. Arseculeratne and G. E. Tennekoon. Toxicol 7(2):159-161, 1969.

A mixture of aflatoxins B₁ and G₁ (260 µg and 90 µg, resp., in 0.2 ml of dimethylsulfoxide, or 300 µg and 380 µg in 0.2 ml propylene glycol), prepared from *Aspergillus flavus*, was admin. i.p. to male rats. After sacrifice 16 or 40 hours later, rat livers were homogenized and the lysosomal fraction was analyzed. There was no significant difference between acid phosphatase released by lysosomes from control and test groups, in vivo or in vitro. Histologic examination of corresponding livers showed definite pathologic lesions, and it was concluded that the lysosome is probably not the mediator of hepatocellular damage due to aflatoxins.

70-671 GROWTH IN VITRO OF CELLS FROM HYPERPLASTIC NODULES OF LIVER INDUCED BY 2-FLUORENYLACETAMIDE OR AFLATOXIN B₁. (E.) Slifkin, M. (Allegheny Gen. Hosp. William H. Singer Mem. Res. Inst., Pittsburgh, Pa.), L. P. Merkow, M. Pardo, S. M. Epstein, J. Leighton and E. Farber. Science 167(3916):285-287, 1970.

Hyperplastic liver nodules (HLN) were induced in male albino Wistar rats, 150-200 g, after feeding with 2-fluorenylacetamide (2-FAA) or aflatoxin B₁ for 15 weeks followed by a basal diet. Cells from the HLN were able to be cultured in vitro and were found to have different growth characteristics from 2-FAA-induced hepatocarcinomas. Cytopathic effects were not observed. Cells from adjacent liver tissue or from liver tissue of controls degenerated in culture after 48 hours.

70-672 REACTIVITY IN VIVO OF THE CARCINOGEN N-HYDROXY-2-ACETYLAMINOFLUORENE: INCREASE BY SULFATE ION. (E.) DeBaun, J. R. (U. Wisconsin Med. Ctr., Madison), J. Y. R. Smith, E. C. Miller and J. A. Miller. Science 167(3915):184-186, 1970.

Sulfate ion (as compared to chlorate, phosphate, acetate or no ion), inj. into male rats (250-300 g; CD-random-bred) pretreated with 0.25 M p-hydroxyacetanilide i.p., then given N-hydroxy-2-acetylaminofluorene (N-hydroxy-AAF): (1) caused 2-3 times more 1- and 3-(methionine-S-yl)-2-acetylaminofluorene bound to liver proteins; (2) increased the binding of labeled N-hydroxy-AAF to ribosomal RNA (109%), protein (89%), and DNA (40%) in the liver; and, (3) increased the toxicity of the carcinogen. The data suggest that 2-acetylaminofluorene-N-sulfate is formed in the rat liver in vivo.

70-673 HYPERPLASTIC AND EARLY NEOPLASTIC LESIONS OF THE LIVER IN RATS OF

VARYING AGES WITH DIETARY-INDUCED CIRRHOSIS. (E.) Reuber, M. D. (NCI, Bethesda, Md.). Tumori 55(2):79-82, 1969.

Male and female inbred Buffalo-strain rats, 4-52 weeks old, were given a high-fat, low-protein diet, deficient in choline. The most advanced lesions were in the 8-week-old male animals (16 rats), 2 with hepatocellular carcinoma, and 14 with hyperplastic nodules. All the female 4-week-old (13), and half the 8 and 24-week-old rats (9-10) had hyperplastic nodules, with one hepatocellular carcinoma developing in the latter 2 groups. Most of the animals with nodules had moderate or severe cirrhosis. The hyperplastic lesions, in periportal regions, were similar to precarcinogenic lesions in animals treated with chemical carcinogens.

70-674 LESIONS INDUCED IN RATS BY INJECTIONS OF 4-NITROQUINOLINE-1-OXIDE. (E.) Mulay, A. S. (NCI, Bethesda, Md.) and R. W. O'Gara. J. Nat. Cancer Inst. 43(3):729-733, 1969.

Osborne-Mendel, Fischer, Wistar, and Marshall rats were inj. (s.c.) 3 times/week with 0.2 ml of 0.25% 4-nitroquinoline-1-oxide (4NQO) to a total of 17.5 mg. Animals appearing moribund or with large tumors were killed and tissues examined for pathological changes. The incidence of tumors (fibrosarcomas) in rats surviving 6 mo. was more than 90%. In addition, all the treated rats of the Osborne-Mendel strain demonstrated an accelerated development of kidney tubule dilatation and hyaline casts. An adenocarcinoma of the intestine was seen in two rats of the Fischer strain. Some pulmonary disease was found in every experimental animal, one of the Marshall strain developing focal proliferation of septal cells, another, an early alveogenic carcinoma.

70-675 INTAKE, TRANSPORT AND METABOLISM OF CARCINOGENIC HYDROCARBONS IN THE RESPIRATORY TRACT. (Ger.) Döntenwill, W. (Cigarette Indust. Sci. Res. Inst., Hamburg, Germany), H. Elmenhorst, G. Reckzeh, H.-P. Harke and L. Stadler. Verh. Deutsch. Ges. Path. 52:401-408, 1968.

Benzpyrene and 7,12-dimethylbenzanthracene were admin. to hamsters in different solvents or as suspensions (Lutrol, sesame oil, aerosol with soot, after soot pretreatment, in water or NaCl soln.) by the intratracheal route. The carcinogen content in the lungs and other organs was determined at different time intervals (by column chromatography and fluorimetry). From numerous experiments it was concluded that truly dissolved carcinogens (in Lutrol or sesame oil) are quickly resorbed from the lungs and even in long-term experiments show less carcinogenic activity than suspended carcinogens which first are slowly dissolved and then slowly

resorbed from the lungs. The resorption and degradation of carcinogens was also markedly inhibited by pretreatment with soot, indicating the significance of the condition of lung tissue in carcinogenesis.

70-676 INDUCTION OF LUNG ADENOMAS IN NEWBORN MICE BY BIS(CHLOROMETHYL) ETHER. (E.) Jargus, J. L. (Hazleton Labs., Inc., Falls Church, Va.), W. H. Reese, Jr. and H. A. Rutter. Toxicol. Appl. Pharmacol. 15(1):92-96, 1969.

Bis(chloromethyl)ether (BCME) and chloromethyl methyl ether (CMME) were admin. s.c. at maximal tolerated doses (12.5 and 125 μ l/kg, resp.) to 4-72-hour-old random-bred ICR Swiss mice. In vehicle (peanut oil)-treated controls, the lung adenoma incidence 6 mo. later was 14%, compared to 45% with BCME, 17% with CMME and 100% with urethan; the mean numbers of tumors/mouse were 0.14, 0.64, 0.21 and 17, resp. The tumor incidence was significantly higher in mice treated with BCME than in the vehicle-treated controls; in mice admin. CMME, the tumor incidence was not significantly above the control value. One adenoma and 1 fibrosarcoma of the inj. site were also seen among 100 BCME-treated mice. Similar results were seen in chronic inhalation experiments using BCME and CMME.

70-677 INTRINSIC FACTORS IN PULMONARY CARCINOGENESIS IN THE MOUSE: EFFECTS OF COMPLETE FREUND'S ADJUVANT. (It.) Ribacchi, (U. Perugia, Italy). Lavori Ist. Anat. Univ. Perugia 29(2):81-91, 1969.

A group of male and female BALB/c mice (Group A + U), aged 34 days, was treated with complete Freund's adjuvant (CFA; 0.1 ml x 1 i.p.), 14 days prior to receiving urethan (U; 1.0 mg/g x s.c.) and 13 days prior to a second, identical course of CFA. A second group (Group U) received U alone, at age 40 days. Only animals surviving more than 380 days were included in the study. All animals developed multiple pulmonary tumors, ranging from 0.1-10.0 mm in diameter. The mean number of pulmonary tumors/mouse in Group CFA and U was 17.1, at an age at sacrifice of 414 days. Comparable calculations for Group U were 10.0 and 435, resp. In Group CFA and U, the mean number of tumors/mouse was 19.7, as compared to 14.8 for males. In Group U, there was no significant difference between males and females. Although the percentage of mice with tumors measuring 1.5 mm in diameter or less was the same in both groups (100%), of the CFA and U mice developed tumors measuring 4.5 mm or more, as compared to only 2 of the U mice. The difference between the 2 groups was progressively greater from 1.6 mm on. However, when tumors measured 1.5 mm in diameter or less, the mean number of tumors/mouse was 5.5 for the CFA and U group, 5.3 for the U group, with the 2 groups approaching 1 another

progressively thereafter and meeting at approximately 2.0 tumors/mouse when tumors measured 3.1 mm or more. There were no morphologic or histologic differences between the 2 groups. In each group, 1 female developed localized mediastinal and pleural metastases and 1 female developed a lymphoma of the thymus.

70-678 COMPARATIVE CHRONIC INHALATION TOXICITY OF BERYLLIUM ORES, BERTRANDITE AND BERYL, WITH PRODUCTION OF PULMONARY TUMORS BY BERYL. (E.) Wagner, W. D. (Bureau Occupat. Safety Health, Cincinnati, Ohio), D. H. Groth, J. L. Holtz, G. E. Madden and H. E. Stokinger. Toxic. Appl. Pharmacol. 15(1):10-29, 1969.

Squirrel monkeys, Charles River-Caesarean-derived and Greenacres Controlled Flora rats, and golden hamsters were exposed to the inhalation of beryl or bertrandite ore dust (15 mg/m³) for up to 23 mo. In the lungs of rats, beryl ore produced atypical proliferative changes by 6 mo., followed by the appearance of tumors in 18/19 by 17 mo., including bronchiolar alveolar cell tumors, adenomas, adenocarcinomas, and epidermoid tumors; bertrandite ore dust resulted in granulomatous pulmonary lesions in all rats by 6 mo. and atypical proliferation. Monkey lungs evinced only a nonspecific phagocytic dust reaction around respiratory bronchioles and small blood vessels. In hamster lungs, both types of ore dust induced atypical proliferation, and bertrandite induced occasional granulomatous lesions. Wt. gain was inhibited only in exposed rats, while mortality was increased in all types of exposed animals. Beryllium was detected in lung, liver, bone, and kidney. The hematological picture was unaltered, and no definite trend in alkaline phosphatase activity was seen in serum, lung, kidney, or spleen. In spite of a high silica content in the ores, no silicotic nodules were observed in the lungs.

70-679 STRUCTURE AND DEVELOPMENT OF THE ASBESTOS BODY. (E.) Suzuki, Y. and J. Churg (Mount Sinai Hosp., New York, N. Y.). Amer. J. Path. 55(1):79-107, 1969.

In the lungs of hamsters admin. soft chrysotile asbestos (1 mg, intratracheally), asbestos bodies formed in the cytoplasm of certain cells, especially the alveolar macrophages and (to a lesser extent) the septal and alveolar epithelial cells. The first stage of asbestos body formation was phagocytosis of small fragments (often less than 1 μ in length and 300 Å in diameter) and their incorporation into cytoplasmic phagosomes. Hemosiderin appeared within the cytoplasm; later, iron micelles were transported from the hemosiderin granules into the phagosomes. These iron micelles were progressively conc. near the fiber, and the protein ground substance along the periphery of the phagosome partially cleared. The essential elements of the asbestos

body were the central fiber, its hemosiderin coat and the investing membrane of the phagosome. Uncoated asbestos fibers, possibly released by the death of the cells before iron coating took place, were still visible after 2 yr. It is suggested that these uncoated fibers may cause progressive pathological changes in the lung by continuing to interact with the cells. The sub-microscopic fibers (less than $1\ \mu$ long) may be responsible for most of the biological effects of asbestos.

70-680 OCCURRENCE OF ASBESTOS NEEDLES IN HUMAN LUNGS. (Ger.) Otto, H. (U. Erlangen-Nurnberg Path Inst., Germany) and J. G. v. Fragstein. Int. Arch. Gewerbepath. 25(3): 193-201, 1969.

Dust samples from 218 lungs (13 occupationally exposed to asbestos, 190 occupationally exposed to different types of dust, mainly in the ceramic and porcelain industry, and 15 normal, non-occupationally exposed lungs) were examined by phase contrast microscopy. In all samples from non-exposed and all except 14 of the 190 dust-exposed samples scant (not more than 4/field) numbers of needle-shaped particles were observed. These were usually less than $10\ \mu$ long, occasionally up to $50\ \mu$. The 14 needle-negative samples were obtained from cases of severe silicosis in which the large quantity and type of dust was determined by type of occupational exposure. Dust from lungs of asbestos-exposed persons contained extremely large numbers of needle-shaped particles of varying length (20-100 μ). The length and number of needles were generally correlated with asbestos bodies found in the histological lung preparation only when needles were over $20\ \mu$ long. In 3 cases where needles were less than $20\ \mu$ long, no asbestos bodies were seen in the histological sections. The diagnostic value of needle-shaped particles in dust from lungs is discussed.

70-681 PATIENT WITH PULMONARY ASBESTOSIS, PLEURAL AND PERITONEAL MESOTHELIOMAS AND HEMATOGENOUS METASTASES. (Dut.) Klaassen, C. H. L. (Municipal Med. Health Serv., Haarlem, Netherlands), O. H. Van Persijn Van Meerten and H. De Jager. Nederl. T. Geneesk. 113(14): 612-614, 1969.

After 32 yr. of working at insulating buildings and 7 yr. of retirement, a 72-yr.-old man who smoked approx. 20 g/day of cigarette tobacco presented with high temperature, chronic dyspnea, cyanosis, hepatomegaly, wt. loss and loss of appetite. Asbestos granules were demonstrable in the sputum. The pt. died 10 days later of a combination of intractable pyrexia (40°C), tracheobronchitis and bronchiolitis. Autopsy confirmed the presence of asbestos-induced mesotheliomas in the pleura and the peritoneum, invading the lungs and metastasized

to 1 kidney, the adjacent adrenal gland, the liver, omentum and vertebrae. Four additional cases of simultaneously occurring pleural and peritoneal mesotheliomas are reported, with asbestos granules demonstrable in the lungs of one.

70-682 CASE OF A PRIMARY MALIGNANT TUMOR OF THE HEART. (Pol.) Maternowska, W. (Skawinska 8, Cracow, Poland) and J. Stachura. Gruzlica 37(3):281-284, 1969.

A 24-yr.-old bricklayer exposed to silicone dust for 6 yr. was hospitalized with a diagnosis of pulmonary silicosis because of pain in the lower left thoracic region and disseminated lesions in the lungs (chest X-rays 3 mo. before admission were normal). No cardiac or other abnormalities were detected. Rapidly worsening condition with severe central nervous system symptoms suggested malignancy with metastases. Autopsy 34 days after admission revealed a primary strongly anaplastic malignant tumor (6 cm diameter) in the right atrium of the heart which seemed to originate from the blood vessel tissue. It was classified as a hemangioendothelioblastoma. Metastases to brain, lungs, ribs, liver, kidney and lymph nodes were present.

70-683 INCIDENCE OF SQUAMOUS METAPLASIA OF THE RESPIRATORY EPITHELIUM IN RELATION TO CIGARETTE SMOKE. A CYTOLOGIC STUDY OF 1000 APPARENTLY HEALTHY MALES. (It.) Maltoni, C. (F. Addarii Inst. Oncol., Bologna, Italy), D. Carretti, C. Canepari and G. Ghetti. Cancro 21(4):349-356, 1968.

A cytologic study of the sputum of 1000 apparently healthy municipal employees of the city of Bologna, including 294/1000 who did not smoke at all and 574/1000 who smoked 1 pack/day or less, confirmed that squamous metaplastic cells were found more frequently in smokers than in non-smokers, increasing in number in direct proportion to the number of cigarettes smoked per day. There appeared to be no relationship between the number of cigarettes smoked per day and the degree of metaplasia exhibited, and no relationship was demonstrable between the length of time a subject had been smoking and the degree of metaplasia exhibited.

70-684 CHROMOSOMES IN BRONCHOSCOPIC BIOPSIES FROM PATIENTS WITH BRONCHIAL ADENOMA, BRONCHOGENIC CARCINOMA, AND FROM HEAVY SMOKERS. (E.) Falor, W. H. (Akron City Hosp. Lymph Res. Lab., Ohio), M. Gordon and O. A. Kaczala. Cancer 24(1):198-209, 1969.

Chromosomal analysis of bronchoscopic biopsy specimens revealed aneuploidy in 1 pt. with a bronchial adenoma and hyperdiploidy with marker chromosomes in 4/4 karyotypable bronchial

carcinomas. Specimens from 3/6 chronic smokers showed hyperplastic epithelium but lacked cells in metaphase for chromosomal analysis.

685 ARYL HYDROCARBON HYDROXYLASE ACTIVITY IN HUMAN PLACENTA FROM CIGARETTE SMOKING AND NONSMOKING WOMEN. (E.) Nebert, D. W., J. Winker and H. V. Gelboin (NCI, Bethesda, Md.). Cancer Res. 29(10):1763-1769, 1969.

The activity of aryl hydrocarbon hydroxylase (AHH) was greater in placentas delivered from 46 smokers than in those from 51 nonsmokers, although AHH activity was detected in placentas of the nonsmokers and was absent or below detectable levels in some smokers. Different segments of the same placenta varied in AHH activity by as much as 35%. A higher level of AHH activity was detectable in 59 placentas assayed within 24 hours of delivery than in 38 assayed within 2-7 days of delivery.

686 ECOLOGICAL SIGNIFICANCE OF HEAVY METAL CONTENT OF CIGARETTES. LEAD, CADMIUM AND NICKEL ANALYSIS OF TOBACCO AND THE GAS AND PARTICULATE PHASE. (Ger.) Szadkowski, D. (U. Erlangen-Nurnberg, Germany), H. Schultze, K.-H. Haller and G. Lehnert. Arch. Hyg. Bakt. 133(1):1-8, 1969.

Tobacco, tobacco smoke (gaseous and particulate phase), ashes and butts from 8 most popular cigarette brands (including 5 filter cigarettes) were analyzed for nickel, cadmium and lead. Total main stream smoke contained (in $\mu\text{g}/\text{cigarette}$) 178 ± 0.123 of Cd, 0.225 ± 0.142 of Ni and 483 ± 0.267 of Pb. It is suggested that the inhaled amount of lead has as little causal importance for the increased rate of arteriosclerosis among smokers as cadmium has for emphysema. However, the inhaled amount of cadmium is not insignificant as far as its possible hypertensive effect is concerned. It also seemed doubtful whether inhaled nickel reaches carcinogenic levels.

687 STUDIES TO DETERMINE THE ACUTE AND CHRONIC TOXICITY OF CIGARETTE SMOKE IN PASSIVELY SMOKING EXPERIMENTAL ANIMALS. (Ger.) Kozeh, G., K. Rücker, H.-P. Harke and W. Stenwill (Inst. Sci. Res. Cigarette Indust., Erlangen, Germany). Arzneimittelforschung 22(2):237-241, 1969.

Star AF/Han rats and BALB/c-Jax mice were more susceptible to the toxic effects of passive inhalation of cigarette smoke than were ICI mice or Syrian golden hamsters. The toxic effects in these animals were primarily due to nicotine (N) and carbon monoxide (CO) content, whose effects appeared to be synergistic. The introduction of oxygen into the chamber lessened the toxic effects of CO. Significant differences

attributable to either charcoal filtering or varying the moisture content of the tobacco could not be demonstrated. The hamsters appeared to metabolize nicotine more rapidly than either rats or mice, with a resulting diminution of toxic effects. Fifty percent of the hamsters exposed to 3 x 60 cigarettes/day (10 min. exposure to the smoke from 60 cigarettes, 3 x day, at 3-hour intervals) died within 1.5 weeks. Comparable tabulations for other exposure schemes were: 3 x 30 = 39 weeks, 2 x 30 = 16+ weeks, 1 x 60 = 39 weeks, 1 x 90 = 30 weeks. Deaths were due to chronic N and CO intoxication, pneumonia, pleural effusion or emphysema. No benign or malignant tumors or any other pathological changes could be demonstrated in any of the organs.

70-688 A STUDY OF THE COMPARATIVE CARCINOGENICITY OF CIGARETTE AND CIGAR SMOKE CONDENSATE ON MOUSE SKIN. (E.) Davies, R. F. (Tobacco Res. Council Labs, Harrogate, England) and T. D. Day. Brit. J. Cancer 23(2):363-368, 1969.

The carcinogenicity of smoke condensates (37.5-300 mg/week in divided paintings) from small cigars, plain cigarettes, and cigarettes of cigar tobacco were compared on the skin of 4-6-week-old female albino mice. Over a period of 52 weeks, the cigar smoke condensate was significantly more carcinogenic to mouse skin than were smoke condensates of plain cigarettes or cigarettes of cigar tobacco, there being no difference between the skin carcinogenicity of the latter 2 types of condensates. The origin of the condensate did not influence the incidence of spontaneous tumors at sites other than skin.

70-689 THE MOUSE SKIN CARCINOGENICITY OF CIGARETTE SMOKE CONDENSATE: FRACTIONATED BY SOLVENT PARTITION METHODS. (E.) Whitehead, J. K. (Tobacco Res. Council Labs., Harrogate, England) and K. Rothwell. Brit. J. Cancer 23(4):840-857, 1969.

Three different fractionation schemes were utilized to separate and concentrate the polycyclic aromatic hydrocarbons (PAH) of cigarette smoke condensate, and various fractions were tested for carcinogenicity by painting 4-6-week-old female albino mice. The 3 fractions containing PAH in the most concentrated forms induced tumors in similar numbers of mice. In 2 of the fractionation schemes, considerable amounts of nonPAH, carcinogenic material were lost due to adsorption or catalytic destruction of the material on silica gel or alumina. It is concluded that the solvent partition methods of fractionation minimize losses of biologically active material and that the unsubstituted PAH are not as important in the carcinogenesis of cigarette smoke condensate as has been thought.

70-690 PATHOLOGY AS RELATED TO TRYPTOPHAN METABOLITE EXCRETION, OCCUPATIONAL HISTORY, AND SMOKING HABITS IN PATIENTS WITH BLADDER CANCER. (E.) Friedell, G. H. (St. Vincent Hosp., Worcester, Mass.), S. W. Burney, J. R. Bell and E. Soto. J. Nat. Cancer Inst. 43(1):303-306, 1969.

The histological characterization of bladder tumors was similar in 10 pts. with abnormal and 39 pts. with normal excretion of tryptophan metabolites. There was no significant difference between the histology of bladder tumors in pts. exposed to industrial carcinogens and those in pts. with no known exposure and between bladder tumors arising in smokers and non-smokers. Since larger numbers of carcinomas composed, in part or totally, of squamous cells came from the group exposed occupationally to carcinogens and the group of smokers, further studies will try to detect significant differences in histological types of tumors arising in groups exposed to different environmental hazards.

70-691 A SKIN TEST FOR CARCINOGENS. (E.) Mackie, B. S. (187 Macquarie St., Sydney, Australia). Aust. J. Derm. 10(2):97-99, 1969.

Whole tobacco smoke condensate (a 10% alcohol soln.) was painted for 3 consecutive days on a 2.5 cm square area of the medial aspect of the left forearm of 7 pts. with bronchogenic carcinoma or chronic inflammatory lung disease, all of whom had been heavy smokers. After 7 days, a biopsy was taken and the dry epidermal density (DED) was measured and compared to that of untreated epidermis from the right arm of the same patient. The mean DED of the treated skin from patients with bronchogenic carcinoma was slightly but significantly larger than that of the non-exposed skin; there was no significant difference in the mean skin densities in a group of 3 patients with inflammatory lung disease.

70-692 EXPERIMENTAL PRODUCTION OF CANCER WITH CIGARETTE TAR. (E.) Reddy, D. G., D. B. Reddy (Guntur Med. Coll., India) and V. D. Edward. Indian J. Med. Res. 57(1):124-127, 1969.

Swiss mice of the Rockefeller Foundation Laboratory strain (which showed no spontaneous skin or visceral tumors) were painted with tar from 2 brands of cigarettes available in India (0.25 ml/dose, approx. equivalent to the tar from 1 cigarette). Some mice were exposed on alternate days to the cigarette tar and heat (58° C for 3 min.). After 5 mo., the mice treated with the tar and heat showed epithelial downgrowths with keratinization; 3/31 mice showed marked epithelial hyperplasia, without invasion or metastases. No malignant tumors were seen in these mice (in contrast to mice treated similarly with cigar tar and heat). After treatment with cigarette

tar alone, the mice showed some epithelial cell hyperplasia. Moderate epithelial hyperplasia was seen in about 33% of 20 mice treated only by heat exposure; the predominant effects of heat were healed ulcerations and destruction of the sebaceous glands and hair follicles.

70-693 VERRUCOUS CARCINOMA OF THE ORAL MUCOSA IN PAPUA-NEW GUINEA. (E.) Cooke, R. A. (Roy. Brisbane Hosp., Queensland, Australia) Cancer 24(2):397-402, 1969.

During 1962-1967 inclusive, 315 cases of oral carcinoma were diagnosed in the Pathology Department, Port Moresby, New Guinea; 29/315 were verrucous carcinoma. Although 50% of the population of New Guinea lives in the highlands, all 29 pts. with verrucous carcinoma (25 men, 4 women) came from the coastal areas, where the betel nut grows and is chewed (without an admixture of tobacco) by 90% of the inhabitants. The high proportion of verrucous carcinomas involving the labial commissures (18/29) may be related to the custom of applying lime to the chewing mixture in the mouth by dipping a stick in lime and wiping it along the buccal mucosa. The smoking habits of the inhabitants of this region have not been adequately determined.

70-694 ENHANCEMENT OF CHEMICAL CARCINOGENESIS IN THE HAMSTER CHEEK POUCH BY PRIOR TOPICAL APPLICATION OF VITAMIN A PALMITATE. (E.) Levij, I. S. (Hadassah U. Hosp., Jerusalem, Israel), J. W. Rwomushana and A. Polliack. J. Invest. Derm. 53(3):228-231, 1969.

The effects of 10-week courses of vitamin A palmitate (VA; 3 doses/week of about 3400 U in paraffin soln.) on cheek pouch carcinogenesis by 6-week courses of 7,12-dimethylbenzanthracene (DMBA; 3 doses/week of 0.5% in paraffin soln.) were studied in male Syrian golden hamsters. After application of DMBA alone, the most advanced lesion present was acanthosis with focal epithelial atypia. The most advanced lesion induced by VA alone was transient focal acanthosis with focal atypia. In animals admin. VA followed by DMBA, 6/8 showed focal intra-epithelial carcinomas and 2/8 showed infiltrating carcinomas of the cheek pouch. VA similarly enhanced DMBA carcinogenesis when admin. after DMBA, or in animals treated simultaneously with VA and DMBA. It is suggested that the potentiating effect of VA may result from its effect on lysosomal membranes.

70-695 SUCCINIC DEHYDROGENASE ACTIVITY IN D.M.B.A. INDUCED EXPERIMENTAL ORAL CARCINOGENESIS IN HAMSTER CHEEK POUCH. (E.) Luthra, U. K. (S. N. Med. Coll. Agra, India), V. P. Bharadwaj, V. L. Lahiri and P. N. Wahi. Indian J. Med. Res. 56(12):1766-1770, 1968.

the normal Syrian hamster cheek pouch, aldehyde dehydrogenase (SDH) activity was found predominantly in the basal cells. In moderately marked dyskeratotic lesions induced by painting with 7,12-dimethylbenzanthracene (0.5% in acetone), a semiquantitative increase in SDH activity was seen in the basal cells. SDH activity was greatest in irregularly distributed cells, most of which were in the basal layer. In well-differentiated carcinomas, SDH activity was variable. In intraepithelial and poorly differentiated carcinomas, however, SDH activity was absent or very poor, suggesting that the subcellular organelle bearing and/or the expression of SDH may not be fully differentiated or developed, as a result of disturbances in cellular morphogenesis.

696 THE EFFECT OF OESTROGEN ON 9,10-DIMETHYL-1,2-BENZANTHRACENE (DMBA)-INDUCED CHEEK POUCH CARCINOMA IN CASTRATED AND NON-CASTRATED MALE SYRIAN GOLDEN HAMSTERS. (E.) H. J. Black, A. (Hadassah U. Hosp., Jerusalem, Israel), I. Charuzy and I. S. Levij. Brit. J. Cancer 23(4):781-786, 1969.

Orchiectomized (orx.), (but not intact) male Syrian hamsters, diethylstilbestrol (1.5 mg i.m. inj./week) enhanced the carcinogenesis induced by 7,12-dimethylbenzanthracene (DMBA; 0.5% x 3/week), beginning simultaneously with estrogen inj.) in the cheek pouches; the enhancing effect of estrogen was evident in orx. hamsters after 12 weeks of treatment. Orx. did not influence DMBA carcinogenesis in the absence of estrogen.

697 INFLUENCE OF ANTILYMPHOCYTE SERUM ON DMBA INDUCTION OR ORAL CARCINOMAS. (E.) Woods, D. A. (Imperial Cancer Res. Fund, London). Nature (London) 224(5216):276-277, 1969.

Hamster cheek pouches of 38 hamsters were painted 3 times/week with 0.5% 7,12-dimethylbenzanthracene (DMBA) in mineral oil; 16 of the 38 received antilymphocyte serum (ALS; 0.25 ml s.c. 3 times/week), followed by 0.1 ml 3 times/week after 7 days, beginning 1-8 days before the initiation of painting. Tumors first appeared during the 10th week in hamsters treated with ALS as compared to the eighth week in painted controls. There was also increased the total number of tumors which developed up to 13 week, when none of the untreated hamsters were well enough to be sacrificed to survive. The painted control group survived the 15-week observation period.

698 2-PHENYLPHENANTHRENE-3,2'-DICARBOXYLIC ACID IS NOT BOUND TO MOUSE SKIN PROTEINS AFTER APPLICATION OF 1,2,5,6-DIBENZANTHRACENE: A PRELIMINARY REPORT. (E.) Diringer, H. (Max Planck Institute, Tübingen, Germany) and C. Heidelberger. Proc. Nat. Acad. Sci. U.S.A. 67(11):2127-2128, 1970.

The carcinogen 1,2,5,6-dibenzanthracene-9,10-¹⁴C was administered topically to 25 female Swiss mice. After 48 hours, the skin proteins were extracted, hydrolyzed, chromatographed, and radioscanned, revealing that 2-phenylphenanthrene-3,2'-dicarboxylic acid is not, as erroneously reported, bound to mouse skin proteins as a metabolite of the carcinogen.

70-699 CONNECTIVE TISSUE RESPONSE TO A SHORT-TERM SERIES OF SUBCUTANEOUS INJECTIONS OF SORBIC ACID OR AFLATOXIN. PHYSICO-CHEMICAL FACTORS DETERMINING REACTION TO SORBIC ACID. (E.) Grasso, P. (British Indust. Biol. Res. Ass., Carshalton, Surrey, England), S. D. Gangolli and J. Hooson. Brit. J. Cancer 23(4):787-799, 1969.

The s.c. inj. of 0.2% aqueous sorbic acid, but not potassium sorbate, in CFE rats led to an initial necrosis of s.c. fat and panniculus carnosus and a reparative connective tissue response, followed by a derangement of this response with atypical foci of fibroblastic proliferation after repeated inj. (2 times/week) at 4-5 weeks. A granulomatous lesion with macrophage necrosis and development of thick collagenous bands containing actively proliferating fibroblasts was induced by s.c. inj. of 0.5 ml of 0.4% sorbic acid in arachis oil, but not by 50 µg aflatoxin in 0.5 ml arachis oil (2 times/week), which produced certain cytologic abnormalities. When 0.4% sorbic acid in arachis oil was mixed in vitro with an equal vol. of distilled water or Kreb's soln., the pH of the aqueous phase fell markedly within 15 min. as sorbic acid diffused into it, suggesting a relationship between sorbic acid-induced lesions in vivo and local tissue pH.

70-700 LACK OF CARCINOGENIC ACTIVITY OF 3-METHYLCHOLANTHRENE IN THE SQUIRREL MONKEY. (E.) Steinmuller, D. (U. Utah Coll. Med., Salt Lake City), L. A. Dillingham and R. T. Prehn. J. Nat. Cancer Inst. 43(5):1175-1180, 1969.

Paraffin disks impregnated with a 5% soln. of 3-methylcholanthrene (MC; 1 disk/25 g body wt., 21-26 disks/animal) were implanted s.c. into 5 adult squirrel monkeys (Saimiri sciureus), and 3 other animals were implanted s.c. with autochthonous skin fragments mixed with crystals of full-strength MC. These 2 methods of MC admin., which induced s.c. tumors in a high frequency in mice, caused no tumors in the squirrel monkeys. At the time of report, 4/8 were alive with no signs of any type of neoplasm, after about 4 yr. of observation, and 4/8 had died of other causes, showing no signs of any neoplastic change at autopsy. Exposure to 5% MC disks was markedly toxic to normal mouse cells in vitro, but had no effect on kidney or muscle cells from squirrel monkeys.

70-701 UTILIZATION OF NEWBORN MICE IN THE
BIOASSAY OF CHEMICAL CARCINOGENS. (E.)

Gargus, J. L. (Hazleton Labs., Inc., Falls Church, Va.), O. E. Paynter and W. H. Reese, Jr. Toxic. Appl. Pharmacol. 15(3):552-559, 1969.

A bioassay for chemical carcinogenicity consisted of s.c. inj. of various test chemicals into 24-72-hour-old ICR Swiss mice, followed 6 mo. later by examination for lung adenomas. The control incidence of adenomas after inj. of the vehicles, saline or peanut oil, was 2-14% with 0.02-0.04 adenomas/mouse. A significantly higher incidence of adenomas (at least twice the control incidence) was induced by urethan (1000-1500 mg/kg), nitrogen mustard (5 mg/kg), and N-nitrosodiethylamine (50 mg/kg), but not by thiourea (2500 mg/kg), mesidine (250 mg/kg), aflatoxin (2.5 mg/kg), croton oil (0.5 ml/kg), DDT (15 g/kg), dodecylbenzene (12.5 ml/kg), or dimethyl sulfoxide (6 ml/kg). Nitrogen mustard in peanut oil or especially in saline, but not in tricaprylin, was positive in this bioassay.

70-702 INFLUENCE OF GERM-FREE STATUS ON
HEPATOMA INDUCTION BY 7,12-DIMETHYL-
BENZ(a)ANTHRACENE IN C3H MICE. (E.) Grant,

G. A. (Chester Beatty Res. Inst., London) and F. J. C. Roe. Nature (London) 222(5200):1282-1283, 1969.

Male C3H mice, maintained in a germ-free (GF; including milk agent-free) status, and male C3H mice from GF litters maintained under "minimal disease" (MD) conditions, were treated with 1 s.c. inj. of 7,12-dimethylbenzanthracene (DMBA) on day 1 or 7 of life (20 and 40 µg, resp.) and sacrificed at age 32-41 weeks. In DMBA-treated mice and in untreated controls, the incidence, multiplicity and size of hepatomas was much less in GF mice than in MD mice, although no marked differences were seen in the incidence of lung adenomas. Several possible explanations for the results are presented, including the role of a hepatoma virus, and the possibly greater ability of immunologically unstressed animals to reject antigenically altered tumor cells, by comparison to mice exposed to a wide range of environmental pathogens.

70-703 EFFECT OF GERM-FREE STATUS AND ANTI-
LYMPHOCYTE SERUM ON INDUCTION OF
VARIOUS TUMOURS IN MICE BY A CHEMICAL CARCINOGEN
GIVEN AT BIRTH. (E.) Grant, G. A. (Chester

Beatty Res. Inst., London) and F. J. C. Roe. Nature (London) 223(5210):1060, 1969.

In female C3H mice, maintained under germ-free (GF) or minimal disease (MD) conditions, no tumors were seen at age 40 weeks in the absence of carcinogen admin. In MD or GF mice, inj. s.c. with 7,12-dimethylbenzanthracene (DMBA; 40 µg) at age 7 days and sacrificed at age 30-34 weeks, lung adenomas were found in 6/34 and 2/10 mice,

resp. (1 MD animal had 2 lung adenomas; the other MD and GF mice had 1 tumor each). No other tumors were found. The results indicated that the GF status had little effect on the tumor incidence at age 30-40-weeks. In mice admin. DMBA (20 µg s.c.) in the first 24 hour of life, and treated with horse anti-mouse lymphocyte serum (ALS; i.p. inj.) repeatedly from 226-269 days of age, no tumors were seen in 17 GF mice sacrificed at age 296 days or in 1 GF mouse that died during ALS admin. In MD mice treated with DMBA and ALS, tumors were seen in 8/17 at age 296 days (hepatoma alone in 1/8, lung adenomas alone in 4/8, both tumors in 1/8, lung adenoma and abdominal sarcoma in 1/8, thymic lymphoma in 1/8), and 2/3 mice dying during ALS admin. showed tumors at autopsy (1 inj.-site sarcoma, 1 lymphoma).

70-704 ELECTRON-MICROSCOPE INVESTIGATION OF
EXPERIMENTAL RHABDOMYOSARCOMA. (E.)

Friedmann, I. (U. London Inst. Laryng. Otol.) and E. S. Bird. J. Path. Bact. 97(2):375-382, 1969.

Female Sprague-Dawley rats were inj. i.m. with suspensions of nickel sulfide or pure nickel (20 mg in saline), which induced rhabdomyosarcomas in 11/30 and 6/25 rats, resp. Latent periods were 125-240 days (av. about 190 days). A comparison of this tumor incidence (about 31%) with the results of previously published studies showed that these Sprague-Dawley rats were somewhat more resistant to the carcinogenic activity of nickel than rats of other strains. The rhabdomyoblasts of these tumors were classified into 4 types, based on the presence or absence of actin and myosin filaments, their distribution and their ultimate organization into sarcomeres and myofibrils. These tumor cells also showed an unusual organelle, the fenestrated sarcoplasmic reticulum (previously noted in some plants and the synchronous muscles of insects), which formed a lattice work of tubules and cisternae enveloping the myofibrils. It is suggested that the fenestrated sarcoplasmic reticulum may be involved in protein and myofilament synthesis.

70-705 CERVICAL DYSPLASIA ASSOCIATED WITH
AZATHIOPRINE (IMURAN) THERAPY. (E.)

Gupta, P. K., V. M. Pinn and P. D. Taft (Massachusetts Gen. Hosp., Boston). Acta Cytol. (Balt.) 13(7):373-376, 1969.

A 22-yr.-old woman with lipoid nephrosis (progressing to chronic membranous glomerulonephritis) of 20 yr. duration was treated with azathioprine (AP; 150 mg/day) after receiving a kidney allograft. Abnormal epithelial cells were seen in the urine after 12-14 days of AP treatment, but not in the 6-day urine specimen. The pt. died 16 days after renal transplantation, showing marked dysplasia of the cervical and vaginal epithelium at autopsy. During the 2 months before death, the pt. had received a

ety of other agents (estrogen and progesterone, methyldopa, antibiotics, analgesics, tranquilizers, vitamin B complex and prednisone), one of which has been reported to be associated with epithelial dysplasias. Two brief courses of nitrogen mustard (4 days each) had been administered at age 12 and 13 yr. No abnormal epithelial cells were found in urine specimens from 25 other treated pts., including 4 adult women.

706 THE POSSIBLE ASSOCIATION OF THE NUCLEIC ACID OF SPERM IN THE INDUCTION OF CERVICAL NEOPLASIA. (E.) Reid, B. L. (University of Sydney, Australia). Cancer Cytol. 8(2):24-25, 1968.

80% of human cervixes, there are 2 periods (prenatal and during the second and third trimesters of the first pregnancy) when the transformation of columnar epithelium to squamous is most active. Cells in the intermediate and early metaplastic stages are phagocytic to sperm, and synthesize nucleic acid consequent to activation and become new epithelium. Tritiated-thymidine-labeled mouse sperm, phagocytized by human metaplastic cells *in vitro*, appeared in the cytoplasm after 6 hr., and in the nucleus after 24 hr. Chromatographic analysis of the host DNA after 24 hr. showed an alteration of the salinity fractionation pattern towards the donor DNA.

707 EXPERIMENTAL HORMONAL CARCINOGENESIS. (It.) Cacciari, P. (St. Anna Hosp. Gynecol., Turin, Italy). Arch. Sci. Med. (Milano) 125(9):453-456, 1968.

Review of the effects of steroid, estrogen and progesterone treatment on the development of experimental mammary tumors in rats and mice is complemented by report of a study in which oophorectomized (oox.) rats receiving estradiol benzoate (0.5 µg/dose, s.c. twice weekly) developed 4 microcarcinomas in response to topical application of chloroform to the cervix, 2 micro- and 6 macrocarcinomas in response to similar topical application of 3-methylcholanthrene (MC) in chloroform (dose, number of rats in each group not stated). Oox. rats receiving estrogens (no details) and treated by topical application of MC to the skin showed a high incidence of cutaneous epidermoid carcinomas. Oox. rats treated with estrogens alone (no details), cervical carcinomas showed decreased alkaline phosphatase, β-hydroxybutyric dehydrogenase and non-specific stearase activity, and significantly increased activity of other enzymes, including 5'-nucleotidase, aminopeptidase, lactic dehydrogenase, glucose-6-phosphate dehydrogenase and others.

708 EFFECTS OF OVARECTOMY ON PRENEOPLASTIC NODULE FORMATION AND MAINTENANCE IN MAMMARY GLANDS OF CARCINOGEN-TREATED RATS.

(E.) Beuving, L. J. (Wistar Inst., Philadelphia, Pa.). J. Nat. Cancer Inst. 43(5):1181-1189, 1969.

The initiation of cellular alterations in the mammary glands of Lewis rats by admin. of 7,12-dimethylbenzanthracene (DMBA; 20 mg x 1) did not require the concomitant action of ovarian hormones, although minimal prior exposure of the host to these hormones might be required. Oophorectomy (oox.) did not affect the survival and maintenance of the premalignant cells, in the form of nodule progenitors, hyperplastic nodules or hyperactive nodule outgrowths. However, studies in oox. animals (with or without "ovarian replacement therapy" by bilateral ovarian grafts) suggested that the ovarian hormones were required for the multiplication of altered cells resulting in the formation of hyperplastic alveolar nodules, as well as for the outgrowth of these nodules and the growth of malignant tumors.

70-709 RESPONSIVENESS OF CARCINOGEN-INDUCED HYPERPLASTIC ALVEOLAR NODULES IN LEWIS RATS TO MAMMARY GLAND GROWTH-REGULATORY MECHANISMS. (E.) Beuving, L. J. (Wistar Inst., Philadelphia, Pa.). J. Nat. Cancer Inst. 43(5):1191-1200, 1969.

Premalignant hyperplastic alveolar nodules, derived from the mammary glands of inbred female Lewis rats 90-150 days after the admin. of 7,12-dimethylbenzanthracene (DMBA; 20 mg once, at age 50-60 days), produced neither outgrowths nor tumors when transplanted into intact mammary glands or s.c. connective tissues of isologous hosts. When transplanted into mammary gland-free fat pads, however, these nodules produced hyperactive outgrowths, which were as responsive as normal mammary epithelial elements to mammary gland growth-regulatory mechanisms. Transplanted mammary carcinomas from DMBA-treated rats grew progressively in all transplantation sites. It is concluded that the premalignant mammary nodules are closer to normal mammary epithelial elements than to mammary tumors in these respects, and that they are similar in behavior to hyperplastic alveolar nodules of mice.

70-710 TUMOR-PRODUCING CAPABILITIES OF HYPERPLASTIC ALVEOLAR NODULES IN VIRGIN AND HORMONE-STIMULATED BALB/c f. C3H AND C3Hf MICE. (E.) Medina, D. (Baylor U. Coll. Med., Houston, Tex.), K. B. DeOme and L. Young. J. Nat. Cancer Inst. 44(1):167-174, 1970.

Hyperplastic alveolar nodules (HAN) developed sporadically and infrequently in mammary tumor virus-positive BALB/c f. C3H virgin female mice, beginning at 35 weeks of age, and more frequently in nodule-inducing virus-positive C3Hf virgin female mice, beginning at 82 weeks of age.

Hormone stimulation by pituitary isografts led to the appearance of HAN after 2 mo. of stimulation in BALB/c f. C3H mice and after 6 mo. of stimulation in C3Hf mice. HAN isologously transplanted into 3-week-old mice of either strain from virgin and hormone-stimulated mice did not differ in their capacity to induce tumors. In BALB/c f. C3H, but not C3Hf mice, hormone stimulation of the host receiving an isologous nodule transplant decreased the mean latent period of tumorigenesis, but did not influence the ultimate tumor incidence.

70-711 INDUCTION OF MAMMARY CANCER AFTER IN VITRO EXPOSURE TO 7,12-DIMETHYLBENZ-[a]ANTHRACENE. (E.) Dao, T. L. (Roswell Park Mem. Inst., Buffalo, N. Y.). Proc. Soc. Exp. Biol. Med. 133(2):416-418, 1970.

The mammary gland was removed unilaterally from female Sprague-Dawley rats (55-60-days-old), incubated *in vitro* for 10 min. with 2.5-30 mg 7,12-dimethylbenzanthracene (DMBA), and autologously reimplanted in the interscapular region of the back. The conc. of DMBA in the treated mammary gland paralleled the conc. of DMBA in the incubation medium, as did the incidence of mammary tumors 4 mo. later, indicating that the carcinogenic effect of DMBA is direct, not through the host.

70-712 MOUSE MAMMARY CARCINOGENESIS BY ETHYL AND BUTYL CARBAMATES. (E.) Garcia, H. (U. Nebraska Coll. Med., Omaha) and A. Guerrero. Proc. Soc. Exp. Biol. Med. 132(2):422-425, 1969.

Virgin female C3H mice (8-10 weeks old; about 18 g) were inj. i.p. with 1% soln. of urethan ethyl carbamate (EC) and butyl carbamate (BC) at various dosage schedules. Fractionated doses of EC increased the incidence of mammary tumors by 14-31%, while a massive dose shortened the latent period and caused an accelerated development of tumors. The difference was inapparent by 52 weeks. BC increased the incidence of tumors by about 23%, and EC and BC together induced a higher incidence than either one alone. Croton oil painted on the skin of animals receiving EC did not induce skin tumors. Animals bearing breast tumors had a higher number of metastases when EC or BC was administered.

70-713 UTERINE, VAGINAL AND MAMMARY TUMOURS INDUCED BY NITROSOUREAS IN PREGNANT RATS. (E.) Alexandrov, V. A. (Res. Inst. Oncol. Lab. Exp. Tumors, Leningrad, USSR). Nature (London) 222(5198):1064-1065, 1969.

Non-inbred white female rats were treated with methylnitrosourea (MNU; i.p.) or ethylnitrosourea (ENU; i.v.) at various times during pregnancy. The MNU doses selected were usually sub-embryo-toxic levels, and the ENU doses were usually the

maximal tolerated doses for embryos at different stages of gestation. In the 2 treatment groups combined, 78/114 rats survived until the first tumor was seen; 24/78 developed a total of 35 tumors, including leiomyosarcomas or neurinomas (schwannomas) of the uterus or vagina (14/24 and 8/24, resp.) and mammary tumors (6/24; 5 fibroadenomas, 1 transplantable adenocarcinoma). Ovarian tumors developed in 3 ENU-treated rats. Four MNU-treated rats showed tumors of other types (1 cerebral spongioblastoma, 1 peripheral neurinoma, 2 adenocarcinomas of the kidney). Multiple tumors developed in 9/24. The usual latent period was at least 1 yr. The only spontaneous tumors seen in untreated controls were rare mammary fibroadenomas and ovarian cysts. It is concluded that the organotropism of the alkylnitrosoureas is shifted from the nervous system to the reproductive organs in rats treated during pregnancy.

70-714 TRANSPLACENTAL ACTIVITY OF CARCINOGENIC SUBSTANCES. ADDITIONAL STUDIES ON ORGAN CULTURES. (Ger.) Shabad, L. M. (Inst. Exp. Clin. Oncol., Moscow). Arzneimittelforschung 19(7):1044-1046, 1969.

Urethan (100-120 mg total dose), N-nitroso-dimethylamine (total dose 50 mg/kg), N-nitroso-N-methylurea (total dose 100 mg/kg), 7,12-dimethylbenzanthracene (DMBA) (2 mg, 6 mg and 10 mg/animal), 3,3'-dichlorobenzidine and o-toluidine (total dose not stated) were admin. either s.c. or p.o. to pregnant female mice of different strains (A1, C₃HA, BALB/c and F1 hybrids (C57xCBA). The embryonal lung and kidney tissue was explanted shortly before birth and cultured. When compared to control cultures, the experimental organ cultures regularly showed a longer life, stimulated proliferation with hyperplasia and focal excrescences. Urethan caused true lung adenoma *in vitro*.

70-715 CANCER OF THE UTERINE CERVIX IN MICE FED A LIQUID DIET CONTAINING AN ANTI-FERTILITY DRUG. (E.) Dunn, T. B. (NCI, Bethesda, Md.). J. Nat. Cancer Inst. 43(3): 671-692, 1969.

Male, 6-mo.-old BALB/c mice (5) were placed on a Metrecal diet for 6 mo. During this time they appeared healthy, had well-formed feces, and their teeth did not grow excessively. Month-old female mice (5) placed on a similar diet, but alternated each week with pellets, averaged a few grams less wt. after the week on liquids. Enovid (0.1 ml of a suspension of 5 mg in 200 ml of saline) was inj. s.c. in newborn BALB/c mice. Autopsies of 19 female mice at 18-25 mo., and 13 male mice at 22-28 mo., showed lesions similar to those of diethylstilbestrol admin. similarly to newborns. Enovid suspended in Metrecal (so that the normal daily consumption of 12-15 ml contained 10-12.5 µg) was provided to

23-day-old female mice. Autopsies 2-4 mo. later showed hyalinization of the endometrial stroma characteristic of the estrogen effect. A suspension of Enovid in the same conc. as above (2-15 ml/day containing 10-12.5 µg) was given to 15 female, 105-day-old mice. Males were placed in the cages after one mo., and 55 days later, one mouse had a litter of two, both dying shortly after birth; another had 2 males and 2 females, all surviving. All mice on Enovid for 18-721 days (6) and 2 of the surviving litter, continued on Enovid for 599 days, were diagnosed as having early and infiltrating cervical cancer. No cervical lesions developed in mice on Enovid alone.

70-716 HISTOCHEMICAL CHARACTERIZATION OF EXPERIMENTAL PROSTATE TUMORS IN MICE INDUCED BY TESTOSTERONE & 20-METHYLCHOLANTHRENE. (E.) Sahu, A. B. (Chittaranjan Nat. Cancer Res. Ctr., Calcutta, India), D. Sinha and B. Mukerji. Indian J. Exp. Biol. 7(1):1-3, 1969.

Fragments of prostatic epithelium from Strain A mice, impregnated with crystals of testosterone and 3-methylcholanthrene, were transplanted s.c. into male Strain A mice. After 6-8 weeks of observation, 40% of the recipients had developed prostatic carcinomas in the tissue grafts. By comparison with normal mouse prostate, these tumors showed elevated levels of acid phosphatase, lipids and periodic acid-Schiff (PAS)-positive mucopolysaccharides, reduced levels of alkaline phosphatase, and unchanged distribution and conc. of DNA and RNA.

70-717 TESTING OF POLYVINYLPYRIDINE-N-OXIDE (PVNO) FOR CARCINOGENIC ACTIVITY IN RATS AND MICE. (Ger.) Schmäh, D. (German Cancer Res. Ctr., Heidelberg). Arzneimittelforschung 19(8):1313-1314, 1969.

PVNO was inj. i.v. at weekly intervals into 48 female 3-mo.-old Wistar rats (20 mg single, 1,500 mg total dose) and into 50 female 2-mo.-old ICI mice (2 mg single, 150 mg total dose). No significant difference in incidence and localization of tumors was seen when compared to controls. Malignant tumors developed in 10% of test rats (4 mammary adenocarcinomas and 1 ovarian carcinoma after an induction period of 90 days) and 8% of control rats, in 34% of test mice (after 200-800 days) and 38% of control mice. It is concluded that the compound is not carcinogenic for these highly cancer-susceptible strains and that it seems to be safe for humans (the large total dose used in the experiment (1,500 mg/kg) corresponds to a total dose of 260 g for humans which is 40 times larger than that given in prophylaxis and therapy of human leukosis.).

70-718 EXPERIMENTAL PRODUCTION OF HYPEROSTOSIS FRONTALIS INTERNA IN MICE. (E.)

Rudali, G. (Curie Found., Paris). Israel J. Med. Sci. 4(6):1230-1235, 1968.

Inbred male mice (strains AkR, R111/f, NLC, C57BL, XVII/G, and F₁ hybrids AkR x R111/f) were thymectomized prior to s.c. implantation of a 5-7 mg cholesterol pellet containing 5% estradiol. Osteomas of the internal table of the skull developed in 3/11 of the F₁ (AkR x R111/f) and in 8/12 of the AkR mice, but in none of the others. In male and female AkR mice, thymectomized at 6 weeks, and given an oral contraceptive (98.5% norethynodrel and 1.5% mestranol in their food at a daily dose of 30 µg/mouse), a high incidence of osteomas of the skull (80-83%) was observed. Gold thioglucose (750 mg/kg i.p.), admin. to thymectomized male and female AkR mice, with and without estradiol treatment, induced osteomas of the skull in all cases, the highest incidence (70%) in those receiving combined treatment. Also noted in these mice were an increased aggressiveness and agitation as well as gross obesity, sterility and other endocrinological disturbances.

70-719 FINE STRUCTURE AND DIFFERENTIATION OF EXPERIMENTAL WILMS' TUMORS. (Ger.) Gusek, W. (U. Hamburg Path. Inst., Germany). Verh. Deutsch. Ges. Path. 52:410-415, 1968.

Nephroblastomas, which appeared to be histologically identical in all respects with Wilms' tumors in man, were induced in young Wistar rats by feeding with cycasin (no additional details). However, in contrast to the human tumor, they were frequently bilateral and/or accompanied by other renal tumors (especially adenomas). Both sarcomatous spindle cells and atypical tubules showed a high degree of alkaline phosphatase and 5'-nucleotidase activity, and both showed very similar ultrastructural and cytologic characteristics, suggesting that the undifferentiated tumor cells, atypical tubules, and sarcomatous spindle cells all had a common origin and were functionally closely related. Pre-existing mesenchymal cells and vascular connective tissue also appeared to be integral parts of the tumor, participating actively in tumor growth and extension. Tubules in the process of formation appeared to be collecting tubules, clearly distinguishable from the multilayered, atypical tubules, and the process was accompanied by the occasional development of rudimentary cilia. In addition to the sarcomatous spindle cells, clearly defined, fibroblastic, interstitial cells, apparently related to a previously reported "interstitial 'Cycasin' tumor" were also evident. Electron microscopic studies of the developing kidney and of early changes induced by feeding "Cycasin" demonstrated simultaneous nucleotoxic changes in undifferentiated stem cells, mesenchymal cells, and angioblasts, appearing to confirm that these nephroblastomas were mixed tumors from the time of their inception.

70-720 THE INDUCTION OF RENAL TUMOURS BY FEEDING BASIC LEAD ACETATE TO MICE AND HAMSTERS. (E.) Van Esch, G. J. (Nat. Inst. Pub. Health, Utrecht, Netherlands) and R. Kroes. Brit. J. Cancer 23(4):765-771, 1969.

Continuous feeding of 0.1% basic lead acetate for 2 yr. or until death to 5-week-old Swiss mice resulted in renal tumors in 7/50, including 3 adenomas and 4 carcinomas. Only 1/50 mice receiving 1.0% basic lead acetate (subsequently reduced to 0.5%) developed a renal tumor, probably because the agent was frequently fatally toxic at this conc. No renal tumors were observed in golden hamsters receiving 0.1% or 0.5% basic lead acetate. In both species, p.o. admin. of basic lead acetate was associated with characteristic non-neoplastic renal alterations, including frequent and pronounced metaplasia of epithelium of Bowman's capsule, enlarged nuclei and acidophilic inclusions in the tubules, cysts, and some dark brown, laminated concretions suggestive of lead deposits. Histologic changes were also noted in other organs.

70-721 ROLE OF COMPENSATORY HYPERPLASIA IN RENAL TUMORS INDUCED IN RATS BY DIMETHYLNITROSAMINE. (It.) Terracini, B. (U. Turin Inst. Anat., Italy), G. Palestro, S. Ruà and A. Trevisio. Tumori 55(6):357-369, 1969.

Among Wistar-Porton rats surviving the effects of 1 s.c. inj. of dimethylnitrosamine (DMN; 125 µg, distilled water), admin. within 24 hours after birth, 20/34 (58.8%) receiving no further treatment showed renal tumors with approx. twice as many anaplastic interstitial as tubular tumors; 13/38 rats also undergoing unilateral nephrectomy (at age of 8-10 weeks) showed renal tumors (34.2%), with approx. equal distribution between these 2 tumor types; 1/38 untreated controls developed an anaplastic interstitial tumor. Hepatic carcinomas were found in 22/34, 16/38 and 0/38, resp. There were no significant differences between treated groups in the mean survival times. Mammary tumors were found in 1/34 non-nephrectomized, treated animals and 5/38 untreated controls. Also found among the controls were pituitary adenomas (5/38), uterine adenocarcinomas (2/38) and 1 case each of uterine sarcoma, adrenal adenoma, unspecified ovarian tumor, and peribronchial pulmonary lymphosarcoma. Among 8-week-old males of the same strain receiving DMN p.o. in drinking water in a conc. of 0.0025% (half the established TD_{50}) for 2 weeks (12/20 with no further treatment, 8/20 sham-nephrectomized on day 8 or 9 of treatment), 0/20 developed renal tumors. Among rats of the same strain and age receiving similar treatment and unilateral nephrectomy on day 7 or 9 of treatment, 0/20 developed renal tumors, although 1/24 undergoing unilateral nephrectomy 2 weeks prior to initiating such p.o. treatment developed a small, cortical renal adenoma. Among these 3 p.o.-treated groups, hyperplasia of the renal

tubules was found in 2/20, 7/20 and 4/24, resp.; pulmonary adenomas in 2/20, 0/20 and 4/24, resp. No untreated controls were reported in connection with this p.o. study. In both s.c.- and p.o.-treated animals, nonmalignant renal tissue changes were somewhat more marked in the nephrectomized animals. It is concluded that unilateral nephrectomy did significantly affect DMN-induced renal carcinogenesis.

70-722 DISTANT METASTASES FROM BETA-NAPHTHYL-AMINE INDUCED VESICAL TUMORS IN DOGS. (E.) Harrison, L. H., C. E. Cox (Bowman Gray Sch. Med., Winston-Salem, N. C.), K. W. Banks and W. H. Boyce. J. Urol. 102(5):586-589, 1969.

Feeding of β -naphthylamine (NA; 400 mg/day for 2 yr.) induced moderately well-differentiated transitional cell carcinomas of the bladder after 9-18 mo. in 4/4 female dogs. These tumors regressed following i.v. and intracavitary admin. of 5-fluorouracil, but later recurred (without further NA admin.). The recurrent tumors were histologically identical to the original tumors. After 23-55 months of further observation, 2/3 evaluable animals had developed lung metastases of the same histology. The bladder tumors were very extensive at autopsy in all animals; 1 dog showed metastases to the renal cortex. No lymph node, spleen or liver metastases were seen.

70-723 INDUCING GENITAL CANCER IN PREGNANT RATS. (Ger.) Ivankovic, S. (Max Planck Inst., Freiburg i. Br., Germany). Arzneimittelforschung 19(7):1040-1041, 1969.

N-Ethylnitrosourea (ENU) admin. in a single dose (5-80 mg/kg i.v. or 40 mg/kg p.o.) to 124 pregnant rats (not specified) resulted in death of 50/124 animals from genital tumors. These included 31 ovarian carcinomas (clear cell carcinoma with trabecular structure), 20 uterine tumors (strongly dedifferentiated sarcomas) and 6 vaginal tumors (3 squamous cell carcinomas and 3 undifferentiated sarcomas). The greatest incidence of tumors was obtained with the higher dosages (50% with 60 mg/kg i.v.) after an av. induction time of 550 days. Since treatment of non-pregnant rats only rarely produces genital tumors it is suggested that they are not the result of organotropic activity of ENU but that the increased sensitivity during functional activity of these organs plays an important part in pathogenesis.

70-724 FURTHER INVESTIGATIONS ON THE PROLIFERATIVE RESPONSE OF MOUSE BLADDER EPITHELIUM TO 4-ETHYLSULPHONYLNAPHTHALENE-1-SULPHONAMIDE. (E.) Dzhiyev, F. K., M. Wood, D. M. Cowen, O. Campobasso and D. B. Clayson (Cancer Res. Annexe, Leeds, England). Brit. J. Cancer 23(4):772-780, 1969.

n 325 10-14-week-old (A x IF)_{F1} mice fed 0.005-0.010% 4-ethylsulfonylnaphthalene-1-sulfonamide (ENS) in their diet for 4 days-80 weeks, bladder papillomas and carcinomas were less frequent than in previously reported studies on (Ab x IF)_{F1} and (C57 x IF)_{F1} mice; only 1 papilloma and 6 carcinomas were seen in 74 female mice surviving ENS treatment for 40 weeks or more, and no tumors in 77 male 40-week survivors. Mammary carcinomas were detected in 30% of females surviving on ENS for 40-65 weeks. Autoradiography with ³H-thymidine detected an acute proliferative response of bladder epithelium after 4 days of treatment with ENS, which subsequently declined to almost normal by 65 weeks; nonepithelial as well as epithelial elements of the bladder were involved in the proliferative process at 4 weeks. Epithelial hyperplasia in females was greater than in males after 4 and 31 weeks of ENS treatment and declined in females after 65 and 80 weeks of treatment.

0-725 TRANSPLANTATION OF THREE RENAL TUMORS INDUCED IN RATS BY DIMETHYLNITROSAMINE. (Fr.) Jasmin, G. (U. Montreal, Canada) and J. L. Iopelle. Int. J. Cancer 4(3):299-311, 1969.

Renal tumors composed in whole (1/3) or in part (2/3) of sarcomatous tissue developed in 3 female Wistar rats, 6-7 mo. after the admin. of dimethylnitrosamine (0.8 mg/100 g/day 6 times, s.c. in sesame oil). Subsequent inoc. of cellular suspensions of these tumors into 3-5-day-old Wistar rats of both sexes (s.c., i.p., or i.v.) for 2 passages and into young adult Wistar rats of both sexes for as many as 5 succeeding passages, confirmed that the take of sarcomatous elements was relatively easy, but epithelial elements disappeared entirely after the second passage. Epithelial tissue in the grafted tumors was always clearly delimited from sarcomatous tissue, and no transitional forms were seen. The tumor growth rate increased progressively with repeated passages, and takes were more successful in males. The structural organization of the tumor tissue became progressively simplified with succeeding takes, tending toward a mesenchymal differentiation resembling that of smooth muscle. Myoid cells were well supplied with myofibrils and perivascular distributions suggested the possibility of evolving pericytes, a finding which was consonant with previously reported studies of the development of mesoblastic nephromas. Following the ninth passage in vitro of a cell culture of 1 of the original tumors, the appearance of clumps of epithelial cells similar to those which are found in dysplastic mesoblastic nephromas induced by dimethylnitrosamine in vivo suggested the preservation of a double cell line in vitro, contrasting with the in vivo disappearance of one of these lines.

70-726 ELECTRON MICROSCOPIC STUDY OF THYROID CELLS UNDER NORMAL CONDITIONS AND DURING CARCINOGENESIS IN GOLDEN HAMSTERS. (Rus.) Akimova, R. N. (Res. Inst. Exp. Clin. Oncol., Kiev, USSR) and L. A. Zotikov. Vop. Onkol. 15(1):68-75, 1969.

Thyroid cells of normal Syrian hamsters and those receiving methylthiouracil (MTU; 15 mg/100 g wt. over 6-14 mo.) were studied by electron microscopy. Development of adenomas and thyroid cancer was evident after 4-6 and 13-16 mo., resp. In adenomas, the cytoplasmic organelles showed irregularly formed ergastoplasmic cisternae; some ribonucleoprotein granules (RNP) were separated from the ergastoplasmic membrane or were irregularly located, while the number of free RNPs increased. The mitochondria were more polymorphic while the size and number of lysosomes increased and showed one or more vacuoles. Tumor cell structure showed changes in the nucleocytoplasmic ratio, irregularly formed nuclei with irregular chromatin distribution, disorganized and decreased ergastoplasm, dilatation of the endoplasmic reticulum cisternae, structural changes in the mitochondria (increase in number and size), increased free polyribosomes, and increased size and number of polymorphic lysosomes (with marked increase in acid phosphatase activity). The plasma cell membrane and basal follicular membrane of those thyroid cells undergoing cancer were changed. It was concluded that structural changes in the cells of malignant thyroid tumors led to morphological dedifferentiation and disturbance of hormone formation, the degree of these changes being directly proportional to the extent of disease progression.

70-727 RADIOIMMUNOASSAY OF RAT PROLACTIN. COMPARISON OF RAT PROLACTIN PREPARATIONS ISOLATED FROM THE "GRANULAR FRACTION" OF PITUITARY TUMOUR TRANSPLANTS AND FROM NORMAL PITUITARY GLANDS. (E.) Kwa, H. G. (Netherlands Cancer Inst., Amsterdam), A. A. van der Gugten and F. Verhofstad. Europ. J. Cancer 5(6):559-569, 1969.

A rat prolactin preparation from the granular fraction of transplants of prolactin-producing pituitary tumor (RPT), and rat prolactin from pooled, frozen, normal pituitary glands (RPN), yielded similar antisera titration curves and competitive inhibition curves in radioimmunoassay procedures. Duplicate radioimmunoassays of 2 rat plasma samples and one pituitary homogenate, using the different prolactin preparations, were comparable when the results were expressed in unit wt. equivalents of the preparation employed. In competitive inhibition studies against RPT or RPN, mouse prolactin was somewhat effective, and bovine prolactin evinced even less competitive activity.

70-728 RADIOIMMUNOASSAY OF RAT PROLACTIN. PROLACTIN LEVELS IN PLASMA OF RATS WITH SPONTANEOUS PITUITARY TUMOURS, PRIMARY OESTRONE-INDUCED PITUITARY TUMOURS OR PITUITARY TUMOUR TRANSPLANTS. (E.) Kwa, H. G. (Netherlands Cancer Inst., Amsterdam), A. A. van der Gugten and F. Verhofstad. Europ. J. Cancer 5(6): 571-579, 1969.

In 25 old female rats, elevated plasma levels of prolactin were correlated with the presence of spontaneous pituitary tumors and the presence of mammary tumors. Weekly implantation of estrone-cholesterol pellets into 4 orchietomized (orx.) male rats led to a rapid rise in plasma prolactin, followed by a further increase during days 110-115, as pituitary wt. also increased progressively. Prolactin levels varied markedly from rat to rat and from time to time 3-21 days after transplantation of estrone-induced pituitary tumors into orx. rats receiving monthly implants of estrone-cholesterol, but were generally max. 2 weeks after transplantation.

70-729 CHROMOSOME ABERRATIONS INDUCED IN RAT BONE MARROW CELLS BY 7,12-DIMETHYLBENZ[a]ANTHRACENE. (E.) Kurita, Y. (Aichi Cancer Ctr. Res. Inst., Nagoya, Japan), T. Sugiyama and Y. Nishizuka. J. Nat. Cancer Inst. 43(3): 635-641, 1969.

The chromosomes of bone marrow cells of 4-week-old, male and female Long-Evans rats were examined at 6-hr. intervals following a single i.v. inj. of 7,12-dimethylbenzanthracene (DMBA), at doses of 15, 30, or 50 mg/kg body wt. After 12 hr., a small rise in frequency of aberrant cells was observed, reaching a max. in 24 hr. Most aberrations in both control and treated rats were chromatid breaks. The percent of aberrant cells was dose-dependent and increased proportionally with the chromatid length. At the highest dose: (1) incidence of aberrant cells varied from 20-68%; (2) females were more susceptible than males; and, (3) many cells demonstrated several chromosomal lesions. The largest telocentric chromosome (C1), which is most frequently involved in DMBA-induced leukemia, was most susceptible to DMBA (25% demonstrated a lesion at 24 hour after inj. with 50 mg/kg DMBA), while lesions on the B1 chromosome were seen in about 16-17% of the cells.

70-730 EXPERIMENTAL PLASMACYTOMA IN THE MOUSE: ULTRASTRUCTURAL STUDY. (It.) Sessa, A. (U. Milan Inst. Clin. Med., Italy), G. Galetti and F. Invernizzi. Boll. Ist. Sieroter. Milan. 48(1):58-74, 1969.

When plasmacytomas originally induced in BALB/c or (NZB/B1 x BALB/c)F1 mice by i.p. inj. of mineral oil were transplanted s.c. into homologous hosts, 2 cell lines developed which differed from one another primarily in terms of the

electron density of the cytoplasm, due to differing densities of the hyaloplasmatic matrix and differing contents of free, dispersed RNA granules. In the "dark line," the endoplasmic reticulum was highly irregular and crowded with fine granular and filamentous material, similar to that which filled the perinuclear cisterna. In the "light line," endoplasmic reticulum was dilated or composed of distended tubules and its content, like that of the perinuclear cisterna, was essentially amorphous. In both lines, many dense granular bodies were seen in the cytoplasm, characterized by single or double membranes and a matrix resembling the cristae of mitochondria. In both lines, the endoplasmic reticulum and perinuclear cisterna contained numerous circular or oval, virus-like particles with the characteristic structure of Bernhard's particle A. Another, somewhat larger, virus-like particle was seen occasionally in the cytoplasm, always in contact with the endoplasmic reticulum. Other anomalies which were observed were typical of almost all neoplastic cells.

70-731 7,12-DIMETHYLBENZ[a]ANTHRACENE-INDUCED MALIGNANT LYMPHOMA IN GERM-FREE MICE. (E.) Kajima, M. (U. Notre Dame Lobund Lab., Ind.). Adv. Exp. Med. Biol. 3:153-161, 1969.

Germ-free male and female Swiss-Webster mice were inoc. s.c. with 0.05 ml sesame oil containing 100 µg of 7,12-dimethylbenzanthracene (DMBA). After 11 weeks, 5/8 of the surviving mice developed malignant lymphoma. Macroscopically there was enlargement of the thymus, spleen and lymph nodes; microscopically, neoplastic cells were identified as the stem cell type or the lymphocytic type. Leukocytosis was observed in 3/5 mice with malignant lymphoma and a local solid tumor (fibrosarcoma) was present in 1 case at the inj. site. Electron microscopic examination revealed type C tumor virus particles in both normal and neoplastic tissue.

70-732 RETICULOSES IN THE RAT. (Fr.) Guérin, M. (Sci. Res. Inst. Cancer, Villejuif, France), I. Chouroulinkov and J.-C. Guillon. Bull. Cancer (Paris) 56(3):309-320, 1969.

A morphological study of reticuloses developing in 14/20,000 Wistar rats of both sexes, more than 8 mo. old, showed that the most common form was a disseminated reticular histiogramulocytosis with relatively marked infiltration of histiocytes into the tissues of the liver, spleen, lymph nodes (in approx. 33% of cases) and, occasionally, the lungs. Differential diagnosis between hematosarcoma and reticulum cell sarcoma was relatively easy. Although no specific etiology could be determined, all animals had been previously subjected to unsuccessful efforts to graft various tumors, or had been treated with various physical and chemical agents capable or possibly capable of

ducing carcinogenesis, etc. In 1/14 affected animals, a female treated with 2 topical applications/week of a benzene soln. of butter yellow for some 19 mo., a tumor of an axillary lymph node suggested Hodgkin's disease, although a resection of the tumor (successful in only 1/10 attempts) developed into a lymphoblastic reticulum cell sarcoma which became a polymorphic reticulum cell sarcoma in a second passage.

-733 ASSOCIATION BETWEEN CHLORAMPHENICOL, HYPOPLASTIC ANEMIA AND ACUTE MYELOBLASTIC LEUKEMIA: A CASE REPORT. (E.) Edwards, D. (U. Illinois Coll. Med., Chicago). Milit. Med. 134(12):1447-1449, 1969.

A 34-yr.-old male American seaman was admitted to the hospital after 12 days of taking 3 capsules/day of 400 mg chloramphenicol, 100 mg dicyclanil guaiacolate, and several vitamins. He had received chloramphenicol otic drops for 6 consecutive mo. 6 yr. prior, and reportedly had a sister who died of leukemia. Early blood studies revealed an aplastic anemia, thrombocytopenia and a toxic effect on granulocytes. Bone marrow histology at autopsy, slightly more than 2 mo. later, was diagnosed as acute myeloblastic leukemia.

-734 REGRESSIVE MEDULLARY APLASIA AND TERMINAL ACUTE LEUKEMIA AFTER TREATMENT WITH CHLORAMPHENICOL. (Fr.) Gadrat, J. (St. Jean Hosp., Toulouse, France), J. Monnier, R. Durand and J. Pris. Ann. Med. Intern 120(10):737-742, 1969.

Approx. 2 mo. after terminating treatment of a urinary infection with massive doses of chloramphenicol (2 g/day 50 times), a 43-yr.-old man presented with peripheral pancytopenia and severe medullary aplasia, both of which responded slowly to treatment. Three yr. later, the pt. appeared to be entirely recovered and remained symptom-free (under continued observation) for approx. 4 yr., except for slight, persistent leukopenia. At the end of this time, the sudden onset of a terminal, acute myeloblastic leukemia was complicated by infarct into the wall of the stomach, with hemorrhoidal thrombosis and necrosis extending to the submucosal tissue in the presence of a pyocyanic bacillary infection (Pseudomonas aeruginosa).

-735 ATMOSPHERIC POLLUTION BY AUTOMOBILE EXHAUST GASES IN LARGE RURAL SETTLEMENTS. (Sov.) Kononova, V. A. (Saratov Sci. Res. Inst. of Hyg., USSR). Gig. Sanit. 34(3):94, 1969.

-736 ESTABLISHING PERMISSIBLE LIMITS FOR CARCINOGENS. (REPORT OF A DISCUSSION.). (Sov.) Miller, S. V. (Inst. Indust. Hyg. Occup.

Dis., Sverdlovsk, USSR), B. A. Katsnel'son and B. T. Velichkovskii. Gig. Sanit. 34(3):84-87, 1969.

70-737 BRONCHIAL REACTIVITY TO CIGARETTE AND CIGAR SMOKE. (E.) Robertson, D. G. (Roy. Postgrad. Med. Sch., London), D. A. Warrell, J. S. Newton-Howes and C. M. Fletcher. Brit. Med. J. 3(5665):269-271, 1969.

70-738 DIETHYL AZODICARBOXYLATE OXIDATION OF SOME CARCINOGENIC ARYLHYDROXYLAMINES TO NITROSO DERIVATIVES. (E.) Brill, E. (U. Miami Sch. Med., Coral Gables, Fla.). Experientia 25(7):680, 1969.

70-739 STUDIES ON CARCINOGENIC AZO DYES. I. SYNTHESIS OF AZO DYES LABELED WITH TRITIUM AT THE SPECIFIC POSITION. (Jap.) Baba, S. (Tokyo Coll. Pharm.), Y. Mori, M. Iwao and S. Iwahara. J. Pharm. Soc. Japan 89(8):1158-1162, 1969.

70-740 AFLATOXIN B₁ IN THE EXCRETION OF AFLATOXIN POISONED RATS. (E.) Chou, M. W. (Nat. Taiwan U. Coll. Med., China) and T. C. Tung. J. Formosan Med. Ass. 68(8):389-391, 1969.

70-741 COMPARISON OF THE MUTAGENIC ACTIVITY OF N-METHYLNITROSOUREA, N,N'-DIMETHYLNITROSOUREA, AND N,N',N'-TRIMETHYLNITROSOUREA. (E.) Gichner, T. (Czechoslovak Acad. Sci., Prague), J. Veleminský and V. Pokorný. Arzneimittelforschung 19(7):1053-1055, 1969.

70-742 INDUCTION OF CYTOPLASMIC AND GENIC RESPIRATORY DEFICIENT MUTANTS IN Saccharomyces cerevisiae BY THE CARCINOGENIC NITROSAMIDE 1-NITROSO-IMIDAZOLIDONE-2. (Ger.) Schwaier, R. (U. Freiburg, Germany). Arzneimittelforschung 19(7):1050-1052, 1969.

70-743 STUDIES ON CARCINOGENIC MECHANISMS OF 4-NITROQUINOLINE 1-OXIDE (4NQO). I. SYNTHESIS OF 4NQO TRITIATED AT THE SPECIFIC POSITION OF BENZENE RING. (Jap.) Baba, S. (Tokyo Coll. Pharm.), H. Suzuki and Y. Oyamada. J. Pharm. Soc. Japan 89(9):1317-1319, 1969.

70-744 FURTHER EVIDENCE FOR FORMATION OF 4-NITROQUINOLINE 1-OXIDE. (E.) Kosuge, T. (Shizuoka Coll. Pharm., Japan), H. Zenda, M. Yokota, H. Sawanishi and Y. Suzuki. Chem. Pharm. Bull. (Tokyo) 17(10):2181-2183, 1969.

70-745 ELECTRONIC PROPERTIES OF N-HETERO-AROMATICS. XXXVIII. CHEMICAL CARCINOGENS. (12) THE INTERACTION OF 4-NITRO-QUINOLINE 1-OXIDE WITH PHENOL AND ITS DERIVATIVES. CHARGE TRANSFER AND HYDROGEN BONDING. (Jap.) Okano, T. (Tohoku U., Sendai, Japan), Y. Sato and S. Takenaka. Yakugaku Zasshi (J. Pharm. Soc. Jap.) 89(7):994-1001, 1969.

70-746 OXIDATION OF CARCINOGENIC AZO DYES. II. OXIDATION OF N,N-DIMETHYL-4-AMINOAZOBENZENE USING CER(IV) SULFATE. (Ger.) Matrka, M. (Res. Inst. Organic Syntheses, Pardubice, Czechoslovakia) and J. Marhold. Coll. Czech. Chem. Commun. 33(12):4273-4282, 1968.

70-747 THE $dAMP-Ag^+$ COMPLEX AND THE SOLUBILIZATION OF BENZO[a]PYRENE. (E.) Green, B. (Roy. Cancer Hosp., Chester Beatty Res. Inst., London), R. B. Homer and G. R. McDonough. Europ. J. Biochem. 11(3):427-434, 1969.

70-748 PRODUCTION OF AFLATOXINS BY Aspergillus flavus CULTURED ON FLUE-CURED TOBACCO. (E.) Pattee, H. E. (North Carolina Agricultural Experiment Station, Raleigh). Appl. Microbiol. 18(5):952-953, 1969.

70-749 RELATIONSHIP OF AFLATOXICOSIS TO Salmonella gallinarum INFECTIONS OF CHICKENS. (E.) Smith, J. W. (North Carolina State U., Raleigh), W. R. Prince and P. B. Hamilton. Appl. Microbiol. 18(5):946-947, 1969.

70-750 ON MECHANISMS AFFECTING SPECIES SUSCEPTIBILITY TO AFLATOXIN. (E.) Portman, R. S. (Schering Corp. Biol. Res. Labs., Bloomfield, N. J.), K. M. Plowman and T. C. Campbell. Biochim. Biophys. Acta 208(3):487-495, 1970.

See also abstract nos.: 557,562,567,568,569,570,571,572,573,574,776,818,819,822,881,888,889,900,901,902,904,911,920,936,951,952,970,971

0-751 SYSTEMATIC ANTIGENIC CHANGE IN HUMAN CARCINOMA TISSUES BY HEMAGGLUTINATION TECHNIQUES. (E.) Björklund, B. (Nat. Bacteriol. Lab., Stockholm). Int. Arch. Allerg. 36(1-2): 91-203, 1969.

Hemagglutination tests, using horse antiserum against HeLa cells, were positive with antigenic preparations of 39/42 (93%) human carcinomas (from 42 Swedish pts.), but only 8/42 normal human tissues (from 14 subjects, mostly in the 0-80 yr. age group), indicating a common antigenicity in human carcinomas, possibly resulting from transformation by a widespread viral agent. Hemagglutination inhibition tests confirmed the statistically significant antigenic difference between human carcinomas and normal tissues.

0-752 DEMONSTRATION OF VIRUS-LIKE PARTICLES IN A BOVINE CELL LINE. (E.) Mussgay, L. (Fed. Res. Inst. Animal Virus Dis., Tubingen, Germany), E. Reczko and R. Ahl. J. Gen. Virol. (3):445-447, 1969.

In sections of subcultures 190-210 of a calf kidney cell line (CK-66 cells), electron microscopic examination revealed 4 types of virus-like particles. Spherical particles resembling those previously reported in BHK 21 cells were observed within the nuclear envelope or in cisternae of the endoplasmic reticulum. Particles resembling elementary bodies of mycoplasmas appeared in the extracellular space. Structures resembling type B and type C particles were rare, but particles resembling the viruses associated with mouse mammary tumors, murine leukemia-lymphoma viruses, Rous sarcoma virus and avian leukosis were seen in some cells. Two types of particles were seen in ultracentrifuged, phosphotungstic acid-stained preparations of tissue culture fluids.

0-753 MALIGNANT LYMPHOMAS OF EXTRATHYMIC ORIGIN INDUCED IN RATS BY MURINE ERYTHROBLASTOSIS VIRUS. (E.) Kirsten, W. H. (U. Chicago, Ill.) and L. A. Mayer. J. Nat. Cancer Inst. 43(3):735-746, 1969.

Wistar/Furth (W/Fu), August, and Long-Evans rats were inoc. with rat-adapted murine erythroblastosis virus obtained from plasma pools of W/Fu rats. High titers of virus, given to rats between 3 and 14 days of age, caused the development of an early response, including erythroblastosis, sarcomas, osteolytic lesions and brain hemorrhages. The late response, characterized by extralymphatic malignant lymphomas, occurred when high titers of virus were inoculated i.p. or i.v. into adult rats, or low doses were given to 3-5-day-old rats. Lymphoma cells could be transplanted to adult rats of the same strain. Deaths from lymphomas occurred between days 47 and 63, while the longest mean

survival time for rats with erythroblastosis was 32 days.

70-754 ERYTHROBLASTOSIS AND ERYTHROBLASTIC LEUKEMIA IN RATS INDUCED BY MATERIAL FROM CHICK ERYTHROBLASTOSIS. (E.) Tobiška, J. (Cancer Res. Inst., Brno, Czechoslovakia), Z. Brada and A. Drozdová. Neoplasma (Bratisl.) 16(5):491-499, 1969.

Inj. i.p. of liver and spleen cells, obtained from chickens with erythroblastosis 22 days after viral inoc., induced tumors in the abdominal cavity in 3/19 newborn Wistar rats and erythroblastic leukemia in 1/19, as discovered at autopsy 11-17 mo. after inj. The tumors in the abdominal cavity were associated with splenic involvement, infiltration of the intestinal wall (2 cases), and formation of vascular granulation tissue which in some sites predominated over cellular elements. The cell types in abdominal tumors and leukemia included erythroblastic cells with one or more globular, pyknotic nuclei and undifferentiated blast cells.

70-755 LEUKEMIA IN GERM-FREE AKR MICE. (E.) Pilgrim, H. I. (U. Utah Germfree Lab., Salt Lake City), R. C. Parks and L. W. Law. Adv. Exp. Med. Biol. 3:125-134, 1969.

Derivation of a germ-free (GF) line of AKR/Lw mice (by foster-nursing on GF Swiss mice) was difficult. Only 1/3 separately derived lines was truly GF; the other 2 lines were contaminated with either Achromobacter delicatulus (this line was discarded) or Corynebacterium murisepticum, apparently by the transplacental route. In conventional (C) and GF AKR mice, the effective leukemia incidence was 100%; any difference between GF and C mice, with respect to the development of leukemia, was too small to be biologically significant. A proctitis syndrome (resembling the "puny disease" described by Pollard) was seen in some GF mice and in some mice contaminated by C. murisepticum. This proctitis had little or no effect on the occurrence of leukemia, although the age at onset of leukemia was higher in male mice with proctitis than in male mice without this syndrome (this was attributed to the stressful effects of the debilitation associated with the syndrome). It is concluded that the development of leukemia in AKR mice (apparently resulting from vertical transmission of a leukemia virus) is not significantly affected by the absence of microbial flora.

70-756 A STUDY CORRELATING VIRUS PARTICLE FREQUENCY WITH DISEASE PROGRESSION IN A TRANSMITTED MURINE LEUKEMIA. (E.) Chapman, A. L. (U. Kansas Sch. Med., Kansas City), H. Cohen, A. H. Nielsen, W. E. Larsen, D. C. Jenkins, W. J. Bopp and A. A. Werder. Proc. Soc. Exp. Biol. Med. 131(3):772-775, 1969.

Axenic, 2-4-day-old CFW_w mice were inoc. i.p. with 0.1 ml of a 20% homogenate of spleen, thymus, lymph nodes and liver from a second-passage CFW_w mouse tumor, derived from a case of spontaneous lymphatic leukemia. Intracytoplasmic type A and type C particles were present in these tissues. Animals were sacrificed at 2-day intervals and tissues examined with the light microscope for leukemic infiltration, and with the electron microscope for viral particles (quantitation of particles was graded 0, no particles, to +4, numerous particles). The 6 animals examined in the first 6 days showed no leukemic infiltration and viral particles from 0 to +2; from days 8-27, 12/14 mice showed leukemic infiltration; 3/12 mice showing early signs showed +3 particles, the remainder showed +4 particles. No leukemic signs were noted in 2 animals examined on days 35 and 36 (particles 0-+1).

70-757 ASSOCIATION OF MURINE LEUKAEMIA VIRUS FROM A MOUSE LYMPHOMA (2731/L) WITH REOVIRUS TYPE 3 INFECTION. (E.) Levy, J. A. (NCI, Bethesda, Md.) and R. J. Huebner. Nature (London) 225(5236):949-950, 1970.

By tissue culture isolation techniques and complement fixation tests, murine leukemia virus (MLV) was detected in 4/5 tumors in Prince Henry mice induced by various means, including one tumor (2731/L) resulting from inoc. with spleen cells from a Prince Henry mouse with a chronic reovirus type 3 infection. Neutralization studies revealed the viral identity to be Gross-AKR in 3/4 tumors; reovirus type 3 could not be detected in any of the tumors. It is suggested that the mouse with chronic reovirus type 3 infection, from which an MLV-containing tumor was derived, harbored MLV in its spleen cells.

70-758 ELECTRON MICROSCOPIC OBSERVATIONS ON THE ASSOCIATION OF VIRUSES WITH MEMBRANE SYSTEMS IN HAMSTER TUMOR CELLS PROPAGATED IN TISSUE CULTURE. (E.) Zeigel, R. F. (Roswell Park Mem. Inst., Buffalo, N. Y.), G. Rabotti and M. V. A. Smith. J. Nat. Cancer Inst. 43(3): 653-669, 1969.

Cell lines from 6 hamster tumors, induced by Bryan strain of Rous sarcoma virus, showed 3 types of virus-like particles by electron microscopy: (1) ring or doughnut-shaped particles (about 70 mμ in diameter), rod-shaped particles (about 2 μ), and characteristic mature virus particles with dense nucleoids, all contained in an area of viroplasm in the cell cytoplasm. These were typical of reovirus particles of various levels of maturity. Particles similar to the doughnut-shape were seen between the outer membrane and the membrane forming the cristae in mitochondria near the viroplasm. The particles were surrounded by a single membrane; (2) a budding particle of electron-dense material

(about 155 mμ diameter) beneath the cell membrane of cells in tissue culture; and (3) particles (about 120 mμ), with a radial internal configuration, singly or in clumps originating by budding from the endoplasmic reticulum. There is no evidence for biological activity in the latter 2 types.

70-759 RAT LEUKEMIA DERIVED 9H VIRUS (9HV). I. PROPERTIES OF THE VIRUS AND EVIDENCE FOR THE DEVELOPMENT OF HETEROGENEITY IN CELL CULTURE. (E.) Eisenstein, S. (U. Miami Sch. Med., Coral Gables, Fla.), V. V. Bergs and M. Bergs. Proc. Soc. Exp. Biol. Med. 131(2): 392-398, 1969.

Two hemagglutinating zones positive for 9H virus (9HV) were seen after ultracentrifugation in a field-formed CsCl gradient: one lighter zone (mean density 1.34), termed the 'B' component (9HV-B); and a heavier (mean density 1.41) 'A' component (9HV-A). Both demonstrated infectious and cytopathic effects on REL cell cultures. Temperature inactivation occurred at 80°C for 9HV-A, and at 86°C for 9HV-B. The heavier 'A' component had some sensitivity to a high pH, while ether and chloroform had no effect. Filtration through Bio-Glas-500 removed the 9HV-B, but propagation in tissue culture (REL rat embryo cells) of the pure 9HV-A gave rise to 80°C-resistant 9HV-B progeny.

70-760 GROWTH OF FELINE LEUKAEMIA VIRUS IN HUMAN CELLS. (E.) Jarrett, O. (U. Glasgow, Scotland), H. M. Laird and D. Hay. Nature (London) 224(5225):1208-1209, 1969.

Four cultures of human embryonic lung cells were inoc. with feline leukemia virus, followed 3 hr. later by replacement of the inocula with medium supplemented with fetal bovine serum. The human cells were subsequently subcultured every 3 days and examined weekly by electron microscopy, which, beginning in the third week, demonstrated continuous viral replication. Viral growth was also detected by the incorporation of ³H-uridine into purified virus from cell culture fluid.

70-761 C-TYPE VIRUS IN BONE MARROW CELLS OF CATS WITH MYELOPROLIFERATIVE DISORDERS. (E.) Herz, A. (U. California Sch. Vet. Med., Davis), G. H. Theilen, O. W. Schalm and R. J. Munn. J. Nat. Cancer Inst. 44(2):339-348, 1970.

Bone marrow cells from 5/5 cats with myeloproliferative disorders (myelofibrosis with or without myeloid metaplasia, erythroleukemia, erythroid hyperplasia with myeloid metaplasia, or erythremic myelosis) contained C-type virus particles morphologically similar to those known as the causal factor of feline lymphosarcoma. No such virus particles were found in bone marrow cells from 3 clinically normal cats.

762 NEUTRALIZATION OF GRAFFI LEUKAEMIA VIRUS. (E.) Levy, J. P. (Saint Louis Sp., Inst. Res. Blood Dis., Paris), B. Varet, Oppenheim and J. C. Leclerc. Nature (London) (5219):606-608, 1969.

Neutralization, cytotoxicity and immunofluorescent studies were performed on Moloney leukemia virus (MLV-M), Graffi leukemia virus (GiLV), cells from mouse lymphomas induced by MLV-M and GiLV (the YC2 and GiC2 lymphomas, resp.), the Moloney and Graffi pseudotypes of mouse sarcoma virus, and mouse L strain cells spontaneously infected with nonleukemic virus, using mouse antisera against these antigenic materials. The results indicated that the viral structural antigens reacting in neutralization studies were different from the cellular "FMRGi" antigen. Antisera against GiLV and rabbit antisera against MLV-M each cross-reacted with both MLV-M and GiLV.

763 ALTERATION OF SKIN IN GROSS LEUKEMIA. I. SYNGENEIC SKIN-GRAFT REJECTION AND TUMOR DEVELOPMENT. (E.) Mariani, T. (Variety Club Heart Hosp., Minneapolis, Minn.), P. B. Hart and R. A. Good. J. Nat. Cancer Inst. (2):319-328, 1970.

Regions of skin, not obviously involved by tumor, were removed from (C3H/BI x DBA/2)F₁ mice with ascites or solid transplantable Gross leukemia virus (GLV)-induced lymphomas, and transplanted into non-tumor-bearing syngeneic mice. Over 7 successive passages, 91% of the recipients rejected these syngeneic grafts and 5% developed tumors at the graft sites. Tumors arising at the graft sites showed the same histological behavior as cells from ascites GLV-induced lymphomas, indicating that the 2 tumors were antigenically similar. "Tumor cells" were found in the donor skin by histological examination, suggesting that graft rejection was caused by the tumor cells. Syngeneic skin grafts from i.v.-inj. preleukemic mice were rejected by the recipients, although no graft-site tumors developed, suggesting that the change in antigenicity might have been caused by the virus rather than by the tumor cells.

764 INHIBITION OF TRANSPLANTED RAT TUMORS BY IMMUNIZATION WITH IDENTICAL TUMOR CELLS INFECTED WITH FRIEND VIRUS. (E.) Hayashi, H. (Hokkaido U. Sch. Med. Cancer Inst., Sapporo, Japan), F. Sendo, H. Kaji, T. Shirai, Saito, N. Takeichi, M. Hosokawa and T. Kodama. Nat. Cancer Inst. 44(1):11-19, 1970.

Mice immunized s.c. with Friend virus-infected tumor cell lines (WST-5, DLT, and KMT-68) did not subsequently sustain s.c. growth of the corresponding transplanted, uninfected tumor cell lines. Friend virus-infected KMT-68 was less tumorigenic than the other 2 infected cell lines;

a high challenge dose (1×10^7) of uninfected KMT-68 was lethal in 2/4. Other immunization procedures, including s.c. inj. of ⁶⁰Co-irradiated tumor cells, s.c. inj. of formalin-killed tumor cells, and temporary growth of tumor cells, were less effective than immunization with Friend virus-infected cells. The results are analyzed and discussed in relation to the possibilities of immunotherapy of tumors with virus-infected tumor cells.

70-765 RAPID CHANGES OF NUCLEASE ACTIVITIES IN SPLEENS OF LEUKAEMIA VIRUS INFECTED MICE. (E.) Chakrabarty, A. K. (Temple U. Sch. Med., Philadelphia, Pa.), H. Friedman and W. S. Ceglowski. Nature (London) 224(5226):1319-1320, 1969.

Nuclease activities were determined in spleens of young adult female BALB/c mice 1-12 days after i.p. inoc. with Friend virus. DNase activity/mg spleen fell rapidly to 20% of control levels by day 3, and returned to near normal between 6-9 days. RNase activity declined slowly but steadily to 5-15% of control levels by days 9-12, paralleling the development of overt leukemic symptoms, and remained depressed throughout the period of infection.

70-766 EFFECT OF A MURINE LEUKAEMIA VIRUS ON "BACKGROUND" ANTIBODY PLAQUE-FORMING CELLS TO SHEEP ERYTHROCYTES AND *E. coli* ANTIGEN. (E.) Hirano, S. (Temple U. Sch. Med., Philadelphia, Pa.) and H. Friedman. Nature (London) 224(5226):1316-1318, 1969.

From 1-14 days after nonimmunized, young adult BALB/c mice were infected i.p. with at least 500 LD₅₀ Friend virus (FV), single-cell suspensions of their spleens were used to determine the number of antibody-plaque forming cells (PFC) to sheep RBC (SRBC) and *E. coli*. The number of PFC to SRBC rose rapidly to 750 PFC/spleen 3 days after infection and remained elevated at 250 PFC/spleen by 14 days; the number was also significantly elevated at 3 days, when calculated on the basis of PFC/million splenic WBC. In contrast, PFC to *E. coli* were not stimulated by FV infection, falling below control levels by 14 days. It is suggested that the viral RNA acts as a nonspecific stimulator of PFC to SRBC.

70-767 EFFECT OF A DNA TUMOUR VIRUS ON ANTIBODY FORMING CELLS IN NEONATALLY INFECTED HAMSTERS. (E.) Friedman, H. (Temple U. Sch. Med., Philadelphia, Pa.) and H. Goldner. Nature (London) 225(5231):455-456, 1970.

Newborn hamsters were inoc. i.p. with SV40 virus, inoc. i.p. with sheep RBC (SRBC) 1-42 days later, and examined for immune responsiveness after a further 4 days. The number of antibody-

plaque forming cells/spleen in infected hamsters was approx. 50% that in controls at 1-2 weeks of age, but was normal thereafter up to 6 weeks of age, while serum antibody responsiveness to SRBC was essentially the same in infected and uninfected hamsters throughout the study. The results demonstrate that the induction of tumor by a DNA virus such as SV40 is not accompanied by significant immunosuppression, in contrast to infection by an RNA leukemia virus.

70-768 DECREASED RATE OF SYNTHESIS OF IMMUNOGLOBULIN (IgG) IN RATS INFECTED WITH MOLONEY LEUKEMIA VIRUS. (E.) Cure, S. F. (California State Dept. Pub. Health, Berkeley) and N. E. Cremer. J. Immun. 102(6):1345-1353, 1969.

The metabolism of IgG in 2-3-mo.-old Osborn-Mendel rats, uninfected or neonatally infected with Moloney leukemia virus (rat-passaged RT34 strain), was studied by i.v. inj. of ^{131}I -labeled IgG, followed by determinations of IgG levels and whole-body and blood radioactivity for 2 weeks. The decreased IgG levels in infected rats resulted from reduced IgG synthesis (5.8 mg/day, compared to 9.1 mg/day), rather than a change in IgG catabolism. The difference in IgG synthesis between infected and uninfected rats was even greater among rats hyperimmunized against ferritin (7.5 mg/day, compared to 53 mg/day).

70-769 MOLONEY LEUKAEMIA VIRUS AS A HELPER IN RETRIEVING FRIEND VIRUS FROM A NON-INFECTIOUS RETICULUM CELL SARCOMA. (E.) Fieldsteel, A. H. (Stanford Res. Inst., Menlo Park, Calif.), C. Kurahara and P. J. Dawson. Nature (London) 223(5212):1274, 1969.

Newborn BALB/c mice were inoc. i.p. with Moloney leukemia virus (MLV), followed 36 days later by s.c. inj. of cultured cells of Friend virus-induced reticulum cell sarcoma (FVTCT). Inoc. i.p. of a 20% cell-free extract of the in vivo tumor, recovered 43-48 days later, induced Friend disease in 30/30 newborn BALB/c mice, while a tumor extract from mice inoc. only with FVTCT induced no evidence of Friend disease in 41 mice. Friend disease was also produced in 16/16 newborn mice inoc. with a 10% cell-free extract from tumor which had been transplanted to weanling BALB/c mice from mice inoc. with FVTCT and MLV.

70-770 MOLONEY LYMPHOMA ANTIBODIES FROM MICE; LOCALIZATION IN SPLEENS OF MOLONEY LYMPHOMA BEARING MICE. (E.) Witz, I. (Tel-Aviv U., Israel), G. Klein and D. Pressman. Proc. Soc. Exp. Biol. Med. 130(4):1102-1105, 1969.

Syngeneic antiserum to Moloney virus-induced lymphomas was prepared by inj. irradiated

lymphoma cells into syngeneic recipients, and labeling the purified antiserum with ^{125}I . Normal isogeneic serum was labeled with ^{131}I . A paired-labeled mixture was inj. into normal and Moloney tumor-bearing mice (ascites YAC tumor) in male A/Sn, A/Hc, and A/St mice; solid YBA tumor in female CBA mice; solid YLI in male C57 Leaden mice. The spleen of the mice with tumors was the only organ showing preferential uptake of the labeled Moloney antiserum. Some questionable fixation was shown by the YAC tumor.

70-771 INDUCTION OF LYMPHATIC LEUKAEMIA IN BALB/c MICE FROM THE ORIGINAL ISOLATE OF RAUSCHER VIRUS. (E.) Fieldsteel, A. H. (Stanford Res. Inst., Menlo Park, Calif.), P. J. Dawson and C. Kurahara. Brit. J. Cancer 23(4): 806-813, 1969.

A splenic extract containing Rauscher virus (from passages 16-18 in BALB/c mice) induced only splenic disease in weanling BALB/c mice and only lymphatic leukemia in C57BL/6 mice and Sprague-Dawley rats. When passaged a varying number of times in rats, the virus produced only lymphatic leukemia when inoc. back into newborn and weanling BALB/c mice. In newborn BALB/c mice, Rauscher's original first passage isolate induced splenic disease in 9/15 and lymphatic leukemia in 3/15, each disease in different animals; subsequent serial passages from donor mice with either disease produced only the donor's disease. Isologous transplantation of a lymphoma from a mouse with lymphatic leukemia was inhibited by immunization with cells from a Friend virus-induced lymphoma in RF mice. The results suggest that Rauscher virus includes 2 viruses, one inducing splenic disease and the other lymphatic leukemia.

70-772 MYELOFIBROSIS IN RATS EXPERIMENTALLY INFECTED WITH A MURINE LEUKAEMIA VIRUS. (E.) van Gorp, L. H. M. (U. Utrecht Inst. Path., Netherlands) and G. J. V. Swaen. J. Path. Bact. 97(2):235-240, 1969.

In Osborne-Mendel rats inj. with Rauscher leukemia virus (RLV) within 3 days after birth and observed for up to 1 yr., the development of RLV-induced lymphatic leukemia, myeloid leukemia or reticulum cell sarcoma was not influenced by splenectomy (splx.), either 1 day before or 1 or 50 days after RLV inj. Myelofibrosis developed in 5/213 rats with RLV-induced lymphosarcoma (2/5; localized to the thymus and regional lymph nodes) or myeloid leukemia (3/5), including 2 intact and 3 splx. animals. The myelofibrosis observed in these rats was histologically similar to myelofibrosis in man. No myelofibrosis was seen in 150 controls. It is suggested that RLV may have induced myelofibrosis in these rats.

0-773 VIRAL INDUCED IMMUNITY TO SYNGENEIC RAUSCHER MURINE LEUKEMIA CELLS, IN THE ABSENCE OF ALLOGENEIC INHIBITION. (E.) Cohen, H. (Massachusetts Gen. Hosp., Boston) and A. Fink. Proc. Soc. Exp. Biol. Med. 132(1): 61-265, 1969.

1H Balb/c mice (both sexes, 8-12 weeks old) were immunized with formalin-treated Rauscher leukemia virus (RLV; 0.25 ml i.p. with Freund's adjuvant; then 0.1 ml s.c. without adjuvant) and attenuated virus from the JLSV 5 tissue culture line (0.05 ml i.p.). The mice were challenged 4 days after the initiation of immunization by i.p. inoc. of malignant ascites cells induced by RLV (0.1 ml). All unimmunized mice died within 2 weeks, whereas 20/24 of the immunized mice were alive after 3 months. Serum and spleen cells from challenged mice were combined with 0.2 ml of malignant ascites cells and inj. s.c. into normal BALB/c mice. The serum and cells had a cytotoxic effect on the transplanted tumor cells, which was eliminated in the spleen cells by X-irradiation (5000 r), or 3 cycles of freezing and thawing. The immune serum was heat-inactivated, but reactivated by addition of guinea pig complement. Normal spleen cells were not rendered ineffective by agglutination to target cells by anti-hemagglutinin. It is suggested that allogeneic inhibition does not play a significant role in transplantation immunity following immunization with killed or attenuated virus.

0-774 STUDIES ON THE SUSCEPTIBILITY OF C57BL/6 MICE TO RAUSCHER VIRUS. I. PROPERTIES OF RAUSCHER VIRUS-INDUCED C57BL/6 LYMPHOMAS. (E.) Ishimoto, A. (Aichi Cancer Ctr. Res. Inst., Nagoya, Japan) and M. Maeda. J. Nat. Cancer Inst. 44(2):361-368, 1970.

Rauscher virus induced lymphomas in 46/113 newborn C57BL/6 mice, and 28 lymphomas were transplantable s.c. into isologous weanling mice while 0 were not. The i.p. inoc. of cell-free extracts of all but one (designated RD-2) of the original 46 lymphomas, induced early hepatosplenomegaly with erythroblastosis in newborn MA and BALB/c mice, and lymphomas in newborn C57BL/6 mice; cell-free extracts of RD-2 (the D-2 having been maintained over 18 mo.) induced only lymphomas in newborn mice of all 3 strains. The leukemogenic activity of virus derived from lymphomas including RD-2, which were transplanted through 12-14 generations, decreased. Friend-Jackson-Rauscher antigen was detected in all lymphomas. Highly diluted Rauscher virus did not induce lymphoma or erythroblastosis in newborn SMA mice.

0-775 INVESTIGATIONS ON THE DEVELOPMENT OF RAUSCHER LEUKEMIA. (Ger.) Seidel, H. J. (Bayer Dye Works Inst. Exp. Path., Wuppertal-Berfeld, Germany). Verh. Deutsch. Ges. Path. 2:398-401, 1968.

Cell-free homogenates of leukemic spleens (0.2 ml of a 10% suspension), inj. i.p. into BALB/c mice (17-19 g), caused leukemia with massive splenomegaly and death after 25-50 days (median survival time 35 days). By day 3 after inj., the red pulp of the spleen, liver and bone marrow showed foci of characteristic large, immature cells with oval nuclei and large nucleoli. These Rauscher cells were classified as proerythroblasts; it is suggested that in the developmental stages of leukemia, maturation of these cells is inhibited and they proliferate in their immature form. Autoradiographic experiments with ³H-thymidine (1.0 µCi/g i.p.) revealed 80-85% labeling of these cells. In the bone marrow a 3-fold increase in the number of megakaryocytes, and in the peripheral blood a significant increase in nucleated cells, was noted. The thymus and lymph nodes were not affected.

70-776 MORPHOLOGICAL TRANSFORMATION OF RAT EMBRYO CELLS INDUCED BY DIETHYLNITROSAMINE AND MURINE LEUKEMIA VIRUSES. (E.) Freeman, A. E. (Microbiol. Ass., Inc., Bethesda, Md.), P. J. Price, H. J. Igel, J. C. Young, J. M. Maryak and R. J. Huebner. J. Nat. Cancer Inst. 44(1):65-78, 1970.

The simultaneous treatment of secondary rat embryo cell cultures with diethylnitrosamine (DNA; 0.1 mM) and either CF-1 or Rauscher C-type RNA murine leukemia virus, followed by repeated feeding with DNA for 21 days, led to morphological transformation between subcultures 6 and 12, consisting of overgrown cultures with randomly-oriented spindle cells. By subculture 43, the cells became aneuploid. These distinct morphologic and chromosomal changes did not appear in cells treated with either virus or DNA alone.

70-777 MULTIPLE ANTIGENIC COMPONENTS OF THE GROUP-SPECIFIC ANTIGEN OF THE AVIAN LEUKOSIS-SARCOMA VIRUSES. (E.) Roth, F. K. (State U. New York, Upstate Med. Ctr., Syracuse) and R. M. Dougherty. Virology 38(2):278-284, 1969.

Antigenic materials, prepared from chick embryo fibroblast cultures infected with avian leukosis-sarcoma viruses (Rous sarcoma, Prague or Schmidt Ruppin strains, or RAV-1), or from leukemic chicken plasma containing avian myeloblastosis virus (BAI strain A), each contained 4 antigenic components, as determined by immunodiffusion and immunoelectrophoresis using group-specific antisera from tumor-bearing hamsters. At least 2/4 of the components were common to both antigenic preparations. Treatment of the antigenic materials with sodium lauryl sulfate, but not ether, was able to alter their diffusion rate and electrical charge. Relatively soluble and insoluble components of the group-specific antigen were demonstrated in centrifugation experiments.

- 70-778 DENSITY OF BAI STRAIN A AVIAN LEUKOSIS VIRUS-ANTIBODY COMPLEXES RELATIVE TO ANTIGEN-ANTIBODY RATIO. (E.) Fritz, R. B. (Duke U. Med. Ctr., Durham, N. C.) and J. W. Beard. J. Immun. 102(5):1326-1329, 1969.

In ultracentrifugation studies of BAI strain A leukosis (myeloblastosis) virus-rabbit antibody complexes on potassium tartrate gradients, the equilibrium density of the virus-antibody complexes was greater than that of the free virus and was directly proportional to the antibody/virus ratio.

- 70-779 RESPONSE OF BONE MARROW TO MC29 AVIAN LEUKOSIS VIRUS IN VITRO. (E.) Langlois, A. J. (Duke U. Med. Ctr., Durham, N. C.), R. B. Fritz, U. Heine, D. Beard, D. P. Bolognesi and J. W. Beard. Cancer Res. 29(11):2056-2074, 1969.

Following *in vitro* inoc. of chicken bone marrow (CBM) with MC29 avian leukosis virus, characteristic altered cells appeared at 5-6 days, but ceased growing after 20 days. Newly liberated virus was detected from 2-10 days by infectivity titration. By light and electron microscopy, the altered CBM resembled myeloid elements of myelomatosis with respect to a low nucleus/cytoplasm ratio, very large nucleoli, and a cytoplasm possessing numerous ribosomes, a "ground glass" appearance, and a dense gray matrix, but differed markedly in these respects from the myeloid cells of myeloblastic leukemia induced by BAI strain A virus. The altered CBM also resembled chick embryo cells infected with MC29 leukosis virus, differing in the quantity and distribution of chromatin.

- 70-780 A HOST-CELL DNA FUNCTION INVOLVED IN THE REPLICATION OF AVIAN TUMOUR VIRUSES AND OF FOWL-PLAGUE VIRUS. (E.) Závada, J. (Imperial Cancer Res. Fund, London). J. Gen. Virol. 4(4):571-576, 1969.

The multiplication of fowl-plague virus (FPV) in chick embryo fibroblasts (CEF) and in hamster embryo cells (HEC) was inhibited by actinomycin D (1.0 µg/ml) and by UV irradiation of the cells, but less so in CEF also infected with avian myeloblastosis virus (BAI strain A) and in HEC transformed by Rous sarcoma virus, than in singly-infected CEF and HEC. The results suggested that avian myeloblastosis virus and Rous sarcoma virus induce products of host cell DNA function which are utilized in the reproduction of FPV.

- 70-781 CHARACTERISTICS OF TWO NEW AVIAN TUMOR VIRUS SUBGROUPS. (E.) Duff, R. G. (Pennsylvania State U. Milton S. Hershey Sch. Med., Hershey) and P. K. Vogt. Virology 39(1): 18-30, 1969.

Certain avian tumor viruses were distinguished from the A and B subgroups by their host range in cultures of 4 genetic types of chicken embryo fibroblasts, by their sensitivity to viral interference by subgroups A and B avian leukosis viruses, and by their antigenicity. A proposed subgroup C consisted of virus B77, Rous-associated viruses types 7 and 49, and a clone-purified line of Prague strain Rous sarcoma virus (RSV). Only virus B77 was oncogenic for newborn hamsters. The proposed subgroup D included cloned derivatives of the Schmidt-Ruppin and Carr-Zilber strains of RSV, Carr Zilber-associated virus, and Rous-associated virus type 50; the sarcoma viruses were highly oncogenic for newborn hamsters. In general, subgroups A and B were propagated in the Western Hemisphere, while subgroups C and D were European.

- 70-782 ENHANCEMENT AND INHIBITION OF AVIAN SARCOMA VIRUSES BY POLYCATIONS AND POLYANIONS. (E.) Toyoshima, K. (U. Washington Sch. Med., Seattle) and P. K. Vogt. Virology 38(3):414-426, 1969.

Certain polycations such as polybrene, when added to chicken embryo fibroblast (CEF) cultures before or at the time of virus inoc., enhanced the infectivity of avian sarcoma viruses, including Rous sarcoma virus (0) and subgroups B, C, and D. The polycations increased the adsorption rate of virus to cell and may also have facilitated viral penetration, but did not affect viral infectivity or viral growth after penetration. Polyanions such as heparin reduced the infectivity of avian sarcoma viruses and neutralized polycation-induced enhancement. However, the polyanion dextran sulfate evinced ambivalent effects, inhibiting infectivity at conc. less than 4 µg/ml but enhancing it at higher conc. Extracts of normal or infected CEF facilitated infectivity, possibly through histones or other basic cell proteins released during freezing and thawing.

- 70-783 THE AFFINITY OF CULTURED CELLS FOR A SILVER SALT AFTER VIRAL INOCULATION. (E.) Lavenda, N. (Wisconsin State U., Oshkosh) and I. Y. Mahmoud. Oncologia (Basel) 23(4): 270-282, 1969.

Three oncogenic viruses (Schmidt-Ruppin Rous sarcoma virus, avian myelomatosis and Bryan high-titer-Rous-associated viruses) and 4 nononcogenic viruses (Newcastle disease, vesicular stomatitis, vaccinia and mumps viruses) were inoc. into cultures of chick fibroblasts and African green monkey kidney cells (Vero cells), resp. After varying periods of incubation, a previously reported staining technique utilizing silver nitrate revealed sparse to dense cytoplasmic particles in infected Vero cells (inoc. with nononcogenic viruses), but not in uninfected

ero cells. Cytoplasmic particles were also observed in both infected (with oncogenic viruses) and uninfected chick fibroblasts, but were densely aggregated in infected fibroblasts and associated with morphological changes such as increased nuclear size and decreased cytoplasm. This staining technique is recommended for the detection of viruses, particularly oncogenic viruses.

0-784 A POSSIBLE SUBUNIT STRUCTURE OF ROUS SARCOMA VIRUS RNA. (E.) Montagnier, J. (Inst. Radium Biol., Orsay, France), A. Goldé and P. Vigier. J. Gen. Virol. 4(3):449-452, 1969.

Unlike ribosomal or encephalomyocarditis virus RNA, Rous sarcoma virus (RSV) RNA was irreversibly dissociated into smaller subunits of approx. equal size, by sedimentation in a 99% dimethyl sulfoxide (DMSO)-sucrose gradient. Since the Bryan strain (associated with an excess of Rous-associated virus particles) and the Schmidt-Ruppin strain of RSV (apparently not associated with a helper lymphoma virus) yielded the same subunits in the presence of DMSO, it is suggested that production of such subunits after DMSO exposure is a feature common to all viruses of the avian leukosis-sarcoma group. The RSV-NA subunits sedimented at 32-34S, indicating a molecular wt. of about 2.5×10^6 daltons. If the configuration of the units in moderate ionic strength resembles that of other single-stranded NA's, the total RSV-RNA molecule would contain such subunits. Evidence is presented to suggest that these subunits correspond to genetic units coding for different components and functions of RSV.

0-785 OCCURRENCE OF PHENOTYPICALLY MIXED VIRUSES IN THE BRYAN HIGH-TITER STRAIN OF ROUS SARCOMA VIRUS AND RSV (RAV-1) STOCKS. (E.) Chung, M. (U. Michigan Sch. Med., Ann Arbor) and R. W. Hinz. Proc. Soc. Exp. Biol. Med. 133(1):20-24, 1970.

Bryan high-titer strain of Rous sarcoma virus (BH-RSV) and its pseudotype RSV (RAV-1) were inoc. into genetically different chick embryo fibroblasts (line 15-1, susceptible to avian tumor virus subgroup A and B (C/O); line 7, resistant to subgroup A (C/A) or both A and B (C/AB)). C/O cells, after preinfection with BH-RSV or its pseudotype passed once through C/A cells, were extremely resistant to superinfection (greater than 100-fold reduced plating efficiency) with BH-RSV or RSV(RAV-1). This suggests that the preinfecting virus carried a virus that interfered with the BH-RSV or RSV(RAV-1). The virus appeared to be antigenically related to RAV-1. Infection of the C/A cells with BH-RSV or its pseudotype resulted in no replication of this RAV-1-related virus, which could reinfect C/O cells but not C/A cells.

It is suggested that the virus was a phenotypically mixed virus with a subgroup A genome enveloped in a subgroup B protein coat. This virus could not infect C/AB cells and was neutralized by group B-specific antiserum.

70-786 RESCUE OF ROUS SARCOMA VIRUS FROM VIROGENIC MAMMALIAN CELLS ASSOCIATED WITH CHICKEN CELLS TREATED WITH SENDAI VIRUS. (E.) Svoboda, J. (Czechoslovak Acad. Sci., Prague) and R. Dourmashkin. J. Gen. Virol. 4(4):523-529, 1969.

In mixed cultures (1:64 or less ratio) of virogenic Chinese hamster cells transformed by Schmidt-Ruppin Rous sarcoma virus (RSCh cells) and chick embryo fibroblasts (CEF) treated with Sendai virus, the amount of rescued Rous sarcoma virus (RSV) decreased linearly with a decrease in RSCh cells (the number of CEF remaining constant), and treatment with Sendai virus increased RSV rescue by a factor of 100. Under various conditions of incubation, the frequency of heterokaryon formation was well correlated with RSV rescue, and cytoplasmic bridges between Sendai-treated RSCh and CEF were observed under the electron microscope. No infectious virus was detected in tissue culture fluid or extracts of RSCh cells when each was incubated with CEF and then treated with Sendai virus.

70-787 KINETICS OF THE DEVELOPMENT OF ROUS SARCOMA VIRUS (SCHMIDT-RUPPIN STRAIN). INCORPORATION OF URIDINE AND ARGININE INTO ASSOCIATED INTRACYTOPLASMIC PARTICLES. HIGH RESOLUTION AUTORADIOGRAPHIC STUDY. (Fr.) Haguénau, F. (Coll. France Exp. Med. Lab., Paris), S. Michelson-Fiske and G. F. Rabotti. C. R. Acad. Sci. [D] (Paris) 270(15):1954-1957, 1970.

In chick fibroblasts transformed *in vitro* by Schmidt-Ruppin strain Rous sarcoma virus and incubated with ^3H -4,5-uridine or ^3H -arginine, incorporation of the 2 precursors into intracytoplasmic A particles was measured at the first-fourth hour. The incorporation of uridine paralleled previously determined incorporation patterns of uridine into C particles, showing a progressive, rapid increase from the second hour on. The incorporation of arginine also showed a progressive increase, beginning with the first-second hour interval, increasing in rate between the second-third hour, and becoming considerably more rapid during the third-fourth hour interval. This was in contrast to the incorporation of arginine into C particles, which plateaued (with slight, hourly variations) from the first hour on. It is concluded that ribonucleoproteins must be present in both A and C, intracytoplasmic particles and that the findings were compatible with the hypothesis that the A particles represented freed nucleocapsids encased within the intermediary membrane of the virus, accumulating in the cytoplasm when the rate of

their formation exceeded the ability of the cellular membrane to absorb them.

- 70-788 IMMUNOLOGICAL STUDIES ON THE MEMBRANE SYSTEMS OF CANCER CELLS. III. IMMUNOSPECIFICITIES OF THE MITOCHONDRIA FROM VIRUS-INDUCED TUMORS BY THE PRECIPITIN REACTION IN AGAR GEL. (E.) Wakabayashi, A. (Okayama U. Med. Sch., Japan). Acta Med. Okayama 23(2):105-124, 1969.

Subcellular fractions from an ascites sarcoma induced in C3H mice by the Schmidt-Ruppin strain of Rous sarcoma virus (the SR-C H/He ascites sarcoma), hamster tumors induced by SV40 or adenovirus type 12, and the AH-130 rat ascites hepatoma, were studied for antigenicity by the agar gel precipitin test, using rabbit antisera. The virus-induced tumors showed no antigenicity common to the mitochondrial and microsomal fractions. The highest antigenicity was found in the mitochondrial fraction. A specific antigenicity was found in the mitochondrial fraction, which was common to all of the virus-induced tumors studied. Tumor mitochondria-specific antigenicity was also found in mitochondria from the AH-130 hepatoma. This specific mitochondrial antigenicity was found in very low levels in mitochondria from regenerating rat liver, but was not found in mitochondria from normal organs (livers of normal or tumor-bearing animals, human liver and spleen or beef heart mitochondria).

- 70-789 INDUCTION OF TRANSPLANTATION RESISTANCE TO ROUS SARCOMA ISOGRAFT BY AVIAN LEUKOSIS VIRUS. (E.) Bauer, H. (Max Planck Inst. Virus Res., Tübingen, Germany), J. Bubenék, T. Graf and C. Allgaier. Virology 39(3):482-490, 1969.

Inbred adult STU mice were immunized with repeated s.c. inj. of $2-5 \times 10^6$ myeloblasts, induced in Shaver chickens by the BAI strain A of avian myeloblastosis virus (AMV), or with repeated inj. of AMV alone. Transplantation resistance was seen when these mice were challenged with isografts of tumors induced by Rous sarcoma virus (RSV). A single s.c. inj. of AMV in newborn STU mice also induced a dose-related resistance to Rous sarcoma cells, whereas uninfected chick embryo fibroblasts, chicken plasma from which AMV had been removed by ultracentrifugation, and non-infectious AMV did not. No common virus-neutralizing capacity was found between the AMV and the RSV. It is suggested that AMV infection of mouse cells may be a requisite for the induction of tumor-specific transplantation antigens (and subsequent immunity to Rous sarcoma isografts).

- 70-790 ROUS SARCOMA VIRUS IN GERM-FREE RATS. (E.) Pollard, M. (U. Notre Dame Lobund Lab., Ind.), M. Kajima and T. P. Zacharia. Adv. Exp. Med. Biol. 3:149-152, 1969.

In conventional or germ-free (GF) newborn Wistar or Sprague-Dawley rats, s.c. inj. of Schmidt-Ruppin strain Rous sarcoma virus (RSV-SR) induced local and sometimes metastatic fibrosarcomas in all animals. The GF rats with RSV-SR-induced tumors showed pathological changes in the liver and spleen resembling those seen in rats with 3-methylcholanthrene- or 7,12-dimethylbenzanthracene-induced tumors. However, no virus particles were detected in the tumor cells from GF rats, and the animals showed no complement-fixing antibodies or antigens related to RSV-SR. The RSV-SR-induced tumors of GF rats were oncogenic in newly hatched chicks or in newborn GF or conventional rats (of the same strain) after inoc. of cell suspensions, but cell-free preparations of these tumors were not oncogenic. The original stock of RSV-SR induced large, virus-containing fibrosarcomas in chicks. It is suggested that the virus may have been defective, requiring an associated virus (not present in the GF animals) for maturation. It is also suggested that some human tumors may show a pattern of activity similar to that seen in these experiments in GF rats.

- 70-791 OVERGROWTH STIMULATING FACTOR RELEASED FROM ROUS SARCOMA CELLS. (E.) Rubin, H. (U. California Virus Lab., Berkeley). Science 167(3922):1271-1272, 1970.

Rous-conditioned medium (RCM) was prepared by culturing 1×10^6 chick embryo (CE) cells in medium containing 1×10^6 focus-forming units of Bryan strain of Rous sarcoma virus. Overgrowth stimulating activity was detectable 4-5 days after infection and increased greatly by 6-7 days. This nonviral factor was not affected by dialysis of cytotoxic substances, sedimentation of the virus, or neutralizing antibody to the virus. The half-life at 60°C was 5 minutes. CE cultures with RCM added showed 3-6 times the incorporation of ^3H -thymidine and the cell number doubled, whereas controls remained the same. This was especially evident in crowded cultures.

- 70-792 ENHANCED VIRUS CONTENT OF CHICKEN TUMOURS INDUCED BY THE SCHMIDT-RUPPIN STRAIN OF ROUS SARCOMA VIRUS. (E.) Smida, J. (Cancer Res. Inst., Bratislava, Czechoslovakia) and V. Smidová. Neoplasma (Bratisl.) 16(4):463-466, 1969.

The Schmidt-Ruppin strain (SR-RSV) of Rous sarcoma virus (RSV), obtained from wing web tumors of SR-RSV-infected 28-47-day-old Brown Leghorn chickens of a leukosis-free strain (with a high prevalence of the C/O cellular phenotype), was passaged by wing web inj. in 14-30-day-old chickens. The SR-RSV-induced tumors showed lower virus contents than tumors induced by Bryan standard RSV or by B77 sarcoma virus; the relatively low virulence of SR-RSV was suggested by the low growth activity of SR-RSV-induced

tumors. Passage 4 SR-RSV tumors showed higher virus contents than passage 1-3 tumors, and a marked increase in the SR-RSV yield was seen in passages 6 and 7. Accidental infection of these chickens by an avian leukosis virus was suggested as a possible cause of the stimulation of virus production in SR-RSV-induced tumors. One experiment in chicks doubly infected with SR-RSV and avian myeloblastosis virus (AMV; inoc. age 10 and 1 day, resp.) gave negative results (no increase in SR-RSV production was seen in chicks inj. with both SR-RSV and AMV), but the results of experiments with other avian leukosis viruses are not described.

793 THE USE OF THE COMPLEMENT FIXATION TEST FOR INDICATION OF SPECIFIC

ANTIGEN IN CHICKEN EMBRYO TISSUE CULTURES WITH THE DIFFERENT SENSITIVITY TO ROUS SARCOMA. (E.) Ivanova, N. A. (All-Union Sci. Res. Inst. of Influenza, Leningrad, USSR), N. P. Lestchinskaya and A. A. Smorodintzev. Neoplasma (Bratisl.) (3):273-277, 1969.

The detection of latent avian leukosis virus in chick embryo fibroblasts by the RIF test and a complement fixation (CF) test was compared in cultures. The RIF test was more sensitive and revealed leukosis infection after fewer cell transfers. The CF antigen was detected in some cultures which remained sensitive to Rous sarcoma virus infection at a given passage level, suggesting that the CF test has a lower specificity.

794 RIFAMPICIN INHIBITS FOCUS FORMATION IN CHICK FIBROBLASTS INFECTED WITH ROUS SARCOMA VIRUS. (E.) Diggelmann, H. (U. Zurich Inst. Molec. Biol., Switzerland) and C. Weissmann. Nature (London) 224(5226):1277-1278, 1969.

Rifampicin (60 µg/ml) moderately suppressed the replication of Rous sarcoma virus (RSV) in chicken embryo fibroblasts (CEF), but was 10 times more effective in inhibiting RSV-induced transformation of CEF. The reduction in focus-forming units could not be attributed to an abortive viral infection or to effects on CEF growth.

795 FRAGMENTATION OF THE NUCLEUS IN ROUS SARCOMA VIRUS-INFECTED CHICK EMBRYO CELLS. II. STRUCTURAL AND METABOLIC STUDIES. (E.) Levinson, W. (U. California Med. Ctr., San Francisco). J. Nat. Cancer Inst. 44(1):151-158, 1970.

Obvious alterations were detected by electron microscopic examination to explain the nuclear fragmentation observed in chick embryo cells infected with Rous sarcoma virus. Protein, DNA and RNA synthesis in infected cells with

fragmented nuclei was at least as good as in cells with normal nuclei. The percentage of cells containing fragmented nuclei increased with increasing multiplicity of infection (MOI), up to a plateau of 7% with an MOI of 0.25. From 3-6 days after infection, the number of cells with fragmented nuclei decreased as the number of transformed cells increased, suggesting that focus formation took place at the site of fragmented nuclei. Autoradiographic studies revealed increased incorporation of thymidine into fragmented nuclei and unaltered incorporation of uridine and leucine. Bromodeoxyuridine enhanced the formation of fragmented nuclei in infected cells.

70-796 CHANGES IN PLOIDY AND TUMORIGENESIS OF RSV-TRANSFORMED RAT FIBROBLASTS EXPOSED TO THYMINE ALKYLAMINE. (E.) Švec, J. J. (Cancer Res. Inst., Bratislava, Czechoslovakia) and D. Šimkovic. Neoplasma (Bratisl.) 16(4):367-375, 1969.

Four or more 0.5-hour exposures to thymine alkylamine (5-bis[2-chloroethyl]amino-6-methyluracil; Ypenyl; 10 µg/ml) markedly diminished the (s.c.) tumorigenicity of Rous sarcoma virus-transformed rat embryo fibroblast (TREF) cultures in homologous rats. This was accompanied by an increase in the chromosomal number of TREF from 62-63 to 104-107. The treated TREF became increasingly resistant to the growth-inhibiting and lethal effects of thymine alkylamine.

70-797 CEREBRAL PHYSIOLOGY IN DOGS AFTER BRAIN-TUMOR INDUCTION WITH SCHMIDT-RUPPIN ROUS SARCOMA VIRUS: EXPERIENCES WITH RADIOIODINATED NORMAL AND ANTIVIRAL IMMUNOGLOBULIN G. (E.) Bigner, D. D. (Duke U. Med. Ctr., Durham, N. C.), R. B. Fritz and E. D. Day. J. Nat. Cancer Inst. 43(3):565-573, 1969.

In dogs bearing Rous sarcoma virus-induced brain tumors, there was little passage into the circulation (3.3% of normal blood levels) of ¹²⁵I-labeled normal canine immunoglobulin G (IgG), inj. into ventricles with a high degree of obstruction ventricular levels were 300 times more than those in cisternal fluid. The levels of IgG from ventricles with little obstruction reached 33% of normal blood levels, and ventricular and cisternal levels were about equal. A comparison of the i.v. and intraventricular routes of inj. showed that hydrocephalus did not block passage into, only out of, the ventricular fluid. Marked differences were found in the distributions of IgG in dogs with virus-induced and kaolin-induced hydrocephalus. The IgG remaining in the brains of normal dogs after intraventricular inj. was mostly confined to the inj. hemisphere (85%); this was not found in hydrocephalic dogs. Antiviral IgG showed the same distribution as normal IgG and was not localized at the tumor site.

70-798 TUMORS OF THE MARMOSET PRODUCED BY ROUS SARCOMA VIRUS. (E.) Levy, B. M. (U. Texas Dent. Sci. Inst., Houston), A. C. Taylor, S. Hampton and G. W. Thoma. Cancer Res. 29(12):2237-2248, 1969.

Rous sarcoma virus (RSV; Schmidt-Ruppin strain) was inj. by various routes (s.c., i.m. or into the mandible and maxilla, spleen, salivary glands or liver) into 25 newborn marmosets (Saguinus oedipus or fuscicollis and Callithrix jacchus). Within 1 mo. after RSV inj., 8/25 died with interstitial pneumonitis (3/8) or enteritis and colitis (5/8), but without tumors. Tumors developed at the site of RSV inj. in 7/17 (45%) of the remaining animals. These tumors were rhabdomyosarcomas, fibrosarcomas and osteosarcomas, depending on the site of RSV inj. Metastases were seen in animals with rhabdomyosarcomas or fibrosarcomas, but not in animals with osteosarcomas.

70-799 IN VITRO PASSAGES OF HAMSTER TUMOUR CELLS INDUCED WITH SCHMIDT-RUPPIN STRAIN OF ROUS SARCOMA VIRUS: THEIR ONCOGENICITY, MORPHOLOGY AND KARYOLOGY. (E.) Smidová, V. (Cancer Res. Inst., Bratislava, Czechoslovakia), V. Ujházy, J. Matoška and J. Smida. Neoplasma (Bratisl.) 15(6):597-606, 1968.

The SHT tumor cell line, derived from anaplastic sarcomas induced in adult hamsters by inj. of cells from chicken tumors induced by the Schmidt-Ruppin strain of Rous sarcoma virus (SR-RSV), was cultivated in vitro for about 500 days. The early in vitro passages consisted of a mixed population of rounded (epithelioid) and fibroblast-like cells. During long-term cultivation, the prevalence of round cells slowly increased; after 500 days, round cells comprised nearly all of each culture. In the early stages, the predominant modal chromosome number was hypodiploid, with occasional near-tetraploid cells. A gradual shift towards aneuploidy was seen during long-term cultivation; in passage 33 (505 days), hypo- and hypertetraploid cells predominated and the original hypodiploid cells had almost disappeared. No changes in chromosomal morphology were seen at any time. The oncogenicity of the SHT cells in adult Syrian hamsters remained unchanged throughout. The SHT cells also retained their oncogenicity for 7-day-old chicks, indicating the persistence of the SR-RSV genome (although no infectious virus could be isolated); this property also remained unchanged throughout the study.

70-800 PECULIARITIES OF COMPLEMENT FIXATION TEST IN HAMSTERS WITH SARCOMA CAUSED BY VARIOUS STRAINS OF ROUS SARCOMA VIRUS. (E.) Lestchinskaya, N. P. (All Union Sci. Res. Inst. Influenza, Leningrad, USSR), N. A. Ivanova and A. A. Smorodintzev. Neoplasma (Bratisl.) 16(3):279-284, 1969.

Rous sarcoma virus strains Schmidt-Ruppin, Bryan, Carr-Zilber, RPL 22.18, and D-5 induced tumors in 93.7%, 54.3%, 22.6%, 14%, and 0% of newborn golden hamsters, resp. Group-specific, complement-fixing antibody to tumor cell antigen or to transformed chick embryo fibroblast antigen was detected in 23.9% of sera from hamsters with Schmidt-Ruppin tumors, 13.3% of sera from hamsters with Bryan tumors, and no sera from other tumor-bearing hamsters. Complement fixing antibody was considerably more frequent among hamsters with large fibrosarcomas (10-30 mm in diameter) or numerous small tumors than among those with a single small tumor.

70-801 STUDIES OF HAMSTER-SPECIFIC ONCOGENIC VIRUS DERIVED FROM HAMSTER TUMORS INDUCED BY KIRSTEN MURINE SARCOMA VIRUS. (E.) Sarma, P. S. (NIH, Bethesda, Md.), T. Log, and R. V. Gilden. Proc. Soc. Exp. Biol. Med. 133(2):718-722, 1970.

A hamster-specific sarcoma virus (HSV), antigenically distinct from Kirsten mouse sarcoma virus (Ki-MSV), was isolated from a transplanted hamster sarcoma line originally induced by Ki-MSV. HSV induced serially transplantable sarcomas in newborn and weanling golden hamsters, but not in newborn DBA/2 or NIH Swiss mice. It also transformed cultures of hamster embryo fibroblasts (HEF), but not mouse embryo fibroblasts, and was released from an established tissue culture line of HSV-transformed HEF.

70-802 HAMSTER-TROPIC SARCOMAGENIC AND NON-SARCOMAGENIC VIRUSES DERIVED FROM HAMSTER TUMORS INDUCED BY THE GROSS PSEUDOTYPE OF MOLONEY SARCOMA VIRUS. (E.) Kelloff, G. (NCI, Bethesda, Md.), R. J. Huebner, Y. K. Lee, R. Toni and R. Gilden. Proc. Nat. Acad. Sci. USA 65(2):310-317, 1970.

From the fourth passage of a transplanted hamster tumor line, originally induced by Gross pseudotype of Moloney sarcoma virus (MSV), a virus was derived which induced sarcomas at or near the inj. site in golden hamsters, but not in NIH Swiss mice, and produced foci by 1-hit kinetics in hamster embryo cells, but not mouse embryo cells. Viral shedding from infected hamster embryo cells, detected by ³H-uridine labeling, suggested the presence of a nonfocus-forming virus. Cocultivation of a culture shedding only the nonfocus-forming virus with HT-1 (MSC-induced hamster tumor) cells yielded virus with focus-forming activity on hamster embryo cells, but not on mouse embryo cells, suggesting, further, that the nonfocus-forming virus performed a helper function. Certain immunological studies indicated that the hamster-specific sarcoma virus was not related to the murine viruses in the original inoculum, but represented indigenous C-type RNA virus of the hamster.

03 REQUIREMENTS FOR RNA AND DNA SYNTHESIS IN THE TRANSFORMATION OF MOUSE EMBRYO SARCOMA BY MURINE SARCOMA VIRUS (MOLONEY). (E.) B. M. (U. Saskatchewan Nat. Cancer Inst., Saskatoon, Canada) and R. Bather. J. Gen. Virol. 457-460, 1969.

hr. pretreatment of mouse embryo cells with actinomycin D or mitomycin C, in conc. which reduced normal or nearly normal rates of cell growth (0.01 µg/ml and 1.0 µg/ml, resp.), greatly inhibited cell transformation by Moloney mouse sarcoma virus and restricted DNA and RNA synthesis, indicating that infection and subsequent transformation in this system are dependent on DNA and RNA synthesis in the host cells. After infection occurred, virus production was little affected by mitomycin C (1.0-10 µg/ml).

04 RESCUE IN VIVO IN ADULT MICE OF MURINE SARCOMA VIRUS (MSV) FROM A NONPRODUCER STRAIN. (E.) Law, L. W. (NCI, Bethesda, Md.) and R. C. Ting. Proc. Soc. Exp. Biol. Med. 133:960-963, 1969.

cells (1.4 - 3 x 10⁵ cells/mouse) from the MSB-1 strain of a BN strain rat were inoc. i.m. into thymectomized (at 3 days), 7-week-old C57BL/6 mice, previously infected (at 3 weeks of age) with Moloney leukemia virus (MLV). Atypical granulomas occurred between days 23 and 85; no tumor was seen in mice receiving MLV alone or in cells alone. Tumors from day 40, 50 and 85 failed to grow in syngeneic recipients, but sections of the tumor contained infectious Moloney sarcoma virus which, at high titers, induced tumors (atypical granulomas) in NIH Swiss mice similar in structure to those from the C57BL/6 mice.

05 MECHANISM INVOLVED IN THE LOSS OF RESPONSE TO THE PROTECTIVE ACTIVITY OF EXOGENOUS INTERFERON IN CELLS INFECTED WITH MURINE SARCOMA VIRUS. (Fr.) Canivet, M. (St. Louis Hosp. Inst. Leukemia Res., Paris), J. Boiron and M. Boiron. C. R. Acad. Sci. [D] (Paris) 268(20):2527-2529, 1969.

control cultures of Swiss mouse embryo cells and cultures infected with Moloney murine sarcoma virus (MSV) showed the same rates of cellular replication. Both incorporated ³H-thymidine at the same rate, and both produced approximately the same number of infectious units of vesicular stomatitis virus (VSV), following VSV infection. In cultures infected with MSV alone, a linear relationship was seen between the amount of interferon produced and the amount of MSV added. UV radiation inhibited cell transformation and interferon production in a similar fashion, as did exposure to heat and inactivation of the culture of a rabbit anti-MSV serum. Interferon was demonstrable in the

culture 3 hours after infection with MSV and became max. at 8 hours. When cultures of mouse fibroblasts were treated with exogenous interferon for 8 hours prior to washing and incubation with MSV or control medium alone, the interferon titer dropped to zero in the MSV-treated cultures when VSV was added 24 hours later, although control cultures did not react similarly. It is concluded that this loss of responsiveness to the protective action of exogenous interferon resulted from an effect of MSV exerted at the stage of transmission of viral messages, rather than that of the penetration of interferon into the cells, the derepression of the cellular genome, or the synthesis of RNA specific for the exogenous interferon.

70-806 EFFECT OF INFECTION WITH MOLONEY SARCOMA AND LEUKEMIA VIRUSES ON NUCLEIC ACID SYNTHESIS IN MOUSE CELL CULTURES. (E.) Hirschman, S. Z. (Mt. Sinai Sch. Med., New York, N. Y.), P. J. Fischinger and T. E. O'Connor. J. Nat. Cancer Inst. 44(1):107-116, 1970.

DNA synthesis (measured by incorporation of ¹⁴C-labeled thymidine) was stimulated in mouse embryo fibroblast cultures (MEF) by infection with Moloney leukemia virus (MLV) or Moloney sarcoma virus (MSV). MSV and MLV stimulated DNA synthesis in 3T3 cells released from growth-inhibition; but not in growth-inhibited 3T3 cells (contact-inhibited cultures). RNA synthesis (³H-uridine incorporation) was not altered by MLV infection in either growth-inhibited or released 3T3 cells.

70-807 NATURE OF COMPETENT VIRAL PARTICLES CONTAINED IN STOCKS OF MOUSE SARCOMA VIRUS, MOLONEY ISOLATE. (Fr.) Guillemain, B. (St. Louis Hosp. Inst. Leukemia Res., Paris), A. Hampe and M. Boiron. C. R. Acad. Sci. [D] (Paris) 269(22):2283-2286, 1969.

When mixed stocks of Moloney murine sarcoma virus (MSV), some unlabeled and some labeled with ³²P, were subjected to a sucrose gradient with an equilibrium of 15-60%, one population of competent MSV was demonstrated at a density of 1.201. Two other peaks, which appeared at 1.173 and 1.181, represented a population of defective MSV and a second population of competent MSV, resp. Additional study confirmed that the competent population at 1.201 was actually composed of defective MSV, "helper" mouse leukemia virus (MLV), and additional competent MSV, such that the total of competent MSV was significantly greater than that found in ordinary stocks. It is concluded that the mixed stocks contained MSV particles which were independently competent and did not depend on the presence of associated MLV particles. These independently competent particles were thought to consist of hybrids which contained the MSV and MLV genomes within

the same envelope, with the genomes becoming dissociated in the course of the vegetative cycle to give rise to defective MSV particles, MLV particles, and new, independently competent, hybrid particles.

- 70-808 IMMUNOTHERAPY AND CHEMOTHERAPY OF MOLONEY SARCOMA VIRUS-INDUCED TUMORS IN MICE. (E.) Fefer, A. (U. Washington Sch. Med., Seattle). Cancer Res. 29(12):2177-2183, 1969.

BALB/c mice with Moloney sarcoma virus (MSV)-induced primary tumors, or inoc. with cells from syngeneic MSV-induced tumors, showed an age-related immunological responsiveness to the tumor antigens. Cyclophosphamide (C) transiently inhibited the growth of both primary and transplanted tumors in young and adult BALB/c mice. In the adult mice, however, no tumor regression was seen because of C-induced immunosuppression. In young BALB/c mice, admin. of spleen cells or serum from adult BALB/c or CDF mice with regressed tumors, alone or combined with C, caused complete regression of primary tumors in some animals. In adult BALB/c mice, the immunosuppressive effect of C was prevented by additional specific immunotherapy, using spleen cells or sera from MSV-hyperimmunized BALB/c, CDF or CBF mice (but not cells from non-immunized mice or an anti-BALB/c serum prepared in C57BL/6 mice). It is concluded that established primary MSV-induced tumors can be cured by lymphoid cells or serum from syngeneic or allogeneic donors specifically sensitized to MSV-induced tumor antigens.

- 70-809 A QUANTITATIVE STUDY ON TRANSFORMATION OF HAMSTER EMBRYO CELLS IN VITRO BY MURINE SARCOMA VIRUSES (HARVEY AND MOLONEY). (E.) Ting, R. C. (NCI, Bethesda, Md.) and A. V. Bader. Virology 39(2):194-204, 1969.

Transformed foci were observed in cultures of hamster embryo cells (HE, from 12-14-day-old PD₄ hamsters) infected with Harvey murine sarcoma virus (MSV-H) or with the Rauscher pseudotype (MSV-RLV), but not with Moloney murine sarcoma virus (MSV-M). Pretreatment of HE cells with diethylaminoethyl-dextran increased the number of foci more than 100-fold. The transformed HE foci released infectious MSV-H or MSV-RLV continuously, as determined in normal rat kidney cell cultures and by direct electron microscopic examination, which showed viruses morphologically similar to type C mouse leukemia viruses budding from plasma membranes. MSV-RLV transformed HE cells with more efficiency than did MSV-H. The s.c. inoc. of 4-wk.-old PD₄ hamsters with HE cells transformed by MSV-RLV or MSV-H induced tumors in 1/4 and 3/4, resp.

- 70-810 DIFFERENT CELL CULTURE CHARACTERISTICS OF TWO STRAINS OF MURINE SARCOMA VIRUS. (E.) Simons, P. J. (U. Western Australia Sch. Med., Perth), S. S. Pepper and R. S. U. Baker. Proc. Soc. Exp. Biol. Med. 131(2):454-456, 1969.

BALB/c mouse embryo cells (CL-1 line) infected with Moloney sarcoma virus (MSV) showed foci of altered cells with distinct cell outlines, made up of both fusiform and round cells. Foci induced with Harvey sarcoma virus (HSV) had large clear areas in their centers and scattered, distinct fusiform and round cells. Subcultures of MSV-altered CL-1 cultures appeared similar to controls, apparently due to a restricted ability of the MSV-transformed cells to divide; the alterations seen in HSV foci spread rapidly in subculture.

- 70-811 INDUCTION OF BONE TUMOURS IN RATS AND HAMSTERS WITH MURINE SARCOMA VIRUS AND THEIR CELL-FREE TRANSMISSION. (E.) Soehner, R. L. (U. Texas M. D. Anderson Hosp., Houston) and L. Dmochowski. Nature (London) 224(5215):191-192, 1969.

Moloney murine sarcoma virus (MSV-M) and Harvey mouse sarcoma virus (MSV-H) in supernatants of tumor homogenates were each inoc. i.p. into 6-day-old NB rats and/or 6-day-old Syrian hamsters. MSV-M virus in 5 passages through NB rats induced tumors of different types at various sites, including bone tumors in all rats with tumors; cell-free filtrates of MSV-M-induced bone tumors also induced bone tumors in NB rats. The i.p. inoc. of a cell-free extract from an MSV-M-induced rat osteosarcoma into hamsters induced soft tissue tumors in 8/14, and 4/8 also developed osteosarcomas. A cell-free extract of an MSV-H-induced Swiss mouse tumor induced bone and other tumors in 8 passages through hamsters. Attempts to transmit bone tumors by cell-free extracts from hamsters into rats were unsuccessful, with or without the use of Moloney leukemia virus as a helper. After the maintenance of MSV-induced rat and hamster bone tumors in tissue culture for 130 days or longer, electron microscopy revealed budding of virus particles from plasma membranes and virus particles morphologically similar to murine leukemia type C virus particles.

- 70-812 TRANSFORMATION AND VIRUS GROWTH BY MURINE SARCOMA VIRUSES IN HUMAN CELLS. (E.) Aaronson, S. A. (NCI, Bethesda, Md.) and G. J. Todaro. Nature (London) 225(5231):458-459, 1970.

Moloney or Kirsten mouse sarcoma viruses transformed 11/18 strains of human fibroblasts, including embryonic lung and kidney, newborn foreskin, and adult skin, although the viruses were considerably more effective on normal rat

ey cells or Balb/3T3 cells than on human s. Transformed foci appeared in the human s as early as 5 days after infection and eased in size during the following week. were still observed after 3 mo. (and 6 sfers); recoverable infectious virus was ble by electron microscopic examination, and acteristic cytoplasmic staining was noted by nofluorescence.

13 MORPHOLOGY OF ASCITES SARCOMA RAB I OF THE MOUSE. (E.) Fritsch, S. (German Sci. Inst. Microbiol. Exp. Therap., Berlin), einecke and W. Jungstand. Neoplasma (tisl.) 16(2):195-204, 1969.

ascites sarcoma RAB I was obtained by i.p. splantation of a spontaneous generalized morphocellular reticulum cell sarcoma in an S BLUHM/Han Jena inbred mouse. The tumor transplantable i.p., s.c. and i.v. to ogous mice and i.p. to homologous, but not rologous, mice. Isologous i.p. transplanta- to 8-10-week-old females was followed by ocytosis after 6 days, tumor infiltrates of toneum and i.p. fatty tissue by the eighth and occasional metastases by day 19. The . of ascites tumor cells depended on the NaCl ent of the diet. Isologous s.c. transplanta- to 9-11-week-old mice led to a less proed leukocytosis, occasional metastasis by 15 and perforation of the epidermis by day . Cell-free filtrates (s.c.) of the ascites rs induced leukemias, mostly myeloid, in 8 surviving isologous newborn mice; the ative agent was identified as Graffi virus ndirect immunofluorescence.

14 IN VIVO STUDIES OF THE FBJ MURINE OSTEOSARCOMA VIRUS. (E.) Kelloff, . (NIH, Bethesda, Md.), W. T. Lane, H. C. er and R. J. Huebner. Nature (London) 521(3):1379-1380, 1969.

susceptibility to tumor induction by FBJ e osteosarcoma virus after neonatal inj. was in C57BL, 40-50% in CF₁, AKR/J, C57Br, and /c, and 90-100% in NIH Swiss and CFW mice. umors were induced in newborn NIH hamsters ewborn Fisher rats. The tumors were palpably , located near the site of inj., accompanied plenomegaly, and histologically characteristic esenchymal sarcomas. Complement fixation s demonstrated group-specific antigen of ne leukemia viruses in homogenates of all ens, all tumors, and occasional thymuses n infected mice. The induction of tumor by virus was prevented in NIH Swiss mice by m from Fisher rats bearing an AKR lympho- oma (16/16 mice after 87 days), by serum an NIH Swiss mouse bearing an FBJ tumor 14), but not by serum from Fisher rats ing M-MSV transplant tumors (3/15), indicating the FBJ virus is a member of the Gross (G+)

or "wild" type subgroup of the murine leukemia viruses.

70-815 IMMUNOLOGIC AND VIRUS STUDIES WITH HUMAN SARCOMAS. (E.) Morton, D. L. (NCI, Bethesda, Md.), R. A. Malmgren, W. T. Hall and G. Schidlovsky. Surgery 66(1):152-161, 1969.

Sera from pts. with osteo- or chondrosarcoma, and from relatives or close associates of these pts., showed osteosarcoma antibodies in 80-92% of indirect immunofluorescence tests (compared to 26% of tests using sera from blood donors). Most of the osteosarcomas apparently contained the same tumor antigen(s). Sera from osteo- sarcoma pts. cross-reacted with soft tissue sarcomas (especially lipo-, fibro- and chondro- sarcomas) and with 2/4 melanomas tested. Permanent cell lines were established from 3/11 human bone or soft tissue sarcomas. One of these cell lines (SA-2 osteosarcoma) originally contained a human embryonic cell-transforming factor and induced leukemias (containing many C-type virus particles) by cell-free extracts in newborn mice. The transforming factor was later lost, and attempts to activate a latent sarcoma virus failed. Electron microscopic examination of tissue cultures of 7 human sarcomas showed immature C-type particles in one liposarcoma. This culture later lost the virus particles, although the cells retained the sarcoma antigen. Examination of tissue specimens from 6 pts. with sarcomas showed intracisternal A-type particles in one chondrosarcoma. It is suggested that an infectious agent is closely associated with some human sarcomas, although its role in the etiology of the tumors is un- known.

70-816 THE STRUCTURE OF THE MAMMARY TUMOR VIRUS. (E.) Calafat, J. (Netherlands Cancer Inst., Amsterdam) and P. Hageman. Virology 38(2):364-368, 1969.

Purified preparations of mammary tumor virus B particles from milk or mammary tumors of BALB/cfC3H or C3H mice were examined with the electron microscope. In thin sections and in ruptured B particles, the following components could be distinguished: spines; a 70 Å thick membrane-like layer; an inner membrane surrounding an eccentric nucleoid. Treatment with 0.1% sodium deoxycholate freed the nucleoid, which appeared like tangled thread and had no subunits or helical structure. Incubation of the B particles with trypsin had no effect on the structure; pepsin produced a dissociation between the envelope and the nucleoid, as did phospholipase C, which also caused the appearance of some ring-like structures and diglyceride-like particles. The nucleoid structure dis- integrated after treatment with trypsin and pepsin, but not RNase.

70-817 MOUSE MAMMARY TUMOR VIRUS (MTV).
EXPERIMENTAL STUDY OF THE STRUCTURE
IN THE EXTRACELLULAR STAGES. GENERAL INTER-
PRETATION OF THE VIRAL CYCLE. (Fr.) Thomas,
J. A. (Ctr. Cell Physiol. Biol. Lab., Paris),
E. Hollande, M. Henry, M.-C. Dutrillaux and C.
Vilain. C. R. Acad. Sci. [D] (Paris) 270(19):
2387-2390, 1970.

In the extracellular phase of the viral cycle of mouse mammary tumor virus (MTV) in the milk and tumor tissue of infected Swiss mice, the internal layer of the viral envelope proved to be a sort of basic armature, composed, at least in part, of lipoproteins. Multiple spicules were attached to it from the outside of the viral body; the helicoidal filament of the nucleocapsid, composed of ribonucleoprotein, was attached to it from the inside, by means of one face of an interposing membrane. Following dehiscence of the envelope, this membrane became itself an envelope for the freed nucleocapsid (Br). The spicules detached themselves from the mature viral particle (Bm) at this time, agglutinated spontaneously for a short time (sometimes into large masses) and then dispersed, leaving the viral body glabrous in an action which could be initiated experimentally by pepsin hydrochloride or ethylenediaminetetracetate (EDTA). EDTA was also capable of initiating dehiscence of the viral envelope (as were phospholipase A and D) and of creating a swelling of the membrane enclosing Br, carrying inflation to the point of rupture and expulsion of the nucleocapsid and its content in the form of tufts, plumes, and masses of varying sizes. In addition to Br, which were found within a few min. of beginning nursing, intact Bm were also found in extracts of milk coagulated in the stomachs of nursing mice. These Bm appeared to be still intact one-half hour after their intubation into the stomachs of adult mice.

70-818 ACTIVATION OF A MAMMARY TUMOUR VIRUS
IN O20 STRAIN MICE BY X-IRRADIATION
AND URETHANE. (E.) Timmermans, A. (Netherlands
Cancer Inst., Amsterdam), P. Bentvelzen, P. C.
Hageman and J. Calafat. J. Gen. Virol. 4(4):
619-621, 1969.

Feeding of urethan to whole body irradiated, 2-mo.-old female O20 mice led to the development of mammary tumors in 4/7 within 1 yr. (0/7 in controls), lymphatic leukemia in 2/7, and a uterine tumor in 1/7. Electron microscopic examination of 1 such mammary tumor revealed budding, mature B particles. The virus from 2 tumors was transmitted by i.p. inj. of cell-free filtrates to 4-week-old female BALB/c mice, producing mammary tumors after 1 yr. in 8/10 and 4/10, resp. (0/447 controls); electron microscopic examination of 3 BALB/c tumors confirmed the presence of B particles. Inj. of O20 female mice with 0.25 ml of 10% urethan induced B particle-containing mammary tumors in 2/16 within 1 yr.

70-819 COMBINED EFFECTS OF 3-METHYLCHOLANTHRENE, MAMMARY TUMOR VIRUS, NODULE-INDUCING VIRUS, AND PROLONGED HORMONAL STIMULATION ON THE TUMOR-PRODUCING CAPABILITIES OF THE NODULE OUTGROWTH LINE D1. (E.) Medina, D. (Baylor U. Coll. Med., Houston, Tex.), L. J. Faulkin, Jr. and K. B. DeOme. J. Nat. Cancer Inst. 44(1):159-15, 1970.

The incidence of mammary tumors from transplanted D1 hyperplastic alveolar nodules was enhanced from 8% (untreated controls) to 50% in BALB/c female mice, by admin. of 3-methylcholanthrene (MCA; 1.0-3.0 mg/week p.o. in divided doses), and further enhanced to 67% by the addition of prolonged hormonal stimulation from pituitary isografts. MCA did not significantly increase the incidence of mammary tumors in D1 nodule-bearing BALB/c f. C3H mice carrying mammary tumor virus (MTV), nor in MTV-carrying BALB/c f. C3H mice receiving prolonged hormonal stimulation. MCA stimulated tumorigenesis from the transplanted nodules in (C3Hf x BALB/c)F₁ carrying nodule-inducing virus.

70-820 STUDIES ON THE ROLE OF THE THYMUS IN
VIRAL TUMORIGENESIS. I. EFFECT OF
THYMECTOMY ON INDUCTION OF HYPERPLASTIC ALVEOLAR
NODULES AND MAMMARY TUMORS IN BALB/cfC3H MICE.
(E.) Heppner, G. H. (U. Washington Med. Sch.,
Seattle), P. C. Wood and D. W. Weiss. Israel J. Med. Sci. 4(6):1195-1203, 1968.

Thymectomy (thmx.) of mammary tumor virus (MTV)-infected female BALB/cfC3H mice, at 1-3 days of age, resulted in a lower incidence of hyperplastic alveolar nodules after noduligenic stimulation with estradiol or deoxycorticosterone acetate (25%, compared to 73.9% in controls). In thmx. multiparous mice, the mean latent period of mammary tumor appearance increased from 9.3 to 11.2 mo. Thmx. did not interfere with virus activity in the blood or with the appearance of active MTV in the milk. Thmx. mice developed more tumors per mouse than controls. The growth of hyperplastic alveolar nodule isografts was supported as well in thmx. mice as in controls.

70-821 STUDIES ON THE ROLE OF THE THYMUS IN
VIRAL TUMORIGENESIS. II. EFFECT OF
THYMECTOMY ON INDUCTION OF HYPERPLASTIC ALVEOLAR
NODULES IN BALB/c MICE INFECTED WITH MAMMARY
TUMOR VIRUS AT VARIOUS AGES. (E.) Heppner,
G. H. (U. Washington Med. Sch., Seattle), P. C.
Wood and D. W. Weiss. Israel J. Med. Sci.
4(6):1204-1209, 1968.

Thymectomized (thmx.; at 1-3 days) BALB/c female mice were infected with mammary tumor virus (MTV) at various ages (1 week-3 mo.), then received a 3-mo. course of stimulation with noduligenic hormones. Thmx. mice infected at ages of 1.5 mo. or older showed a higher incidence of preneoplastic alveolar nodules than

thymx. controls; below the age of 1 mo., the reverse was true. Neither age nor thmx. affected the noduligenic activity of the blood.

822 MAMMARY TUMOR VIRUS (MTV) VIRIONS IN A TRANSPLANTABLE EPENDYMOBLASTOMA. (E.) Laing, D. H. (Inst. Med. Res., Camden, N. J.), Charney, E. Y. Lasfargues, N. H. Sarkar, R. C. and R. P. Ames. Proc. Soc. Exp. Biol. 132(1):125-127, 1969.

In section and negative contrast electron microscopic examination of tissue from a methylcholanthrene-induced ependyoblastoma from a C57BL/6J mouse showed intracytoplasmic primary tumor virus (MTV) virions (B particles). A concentrate of 2 g of tumor was tested against rabbit anti-MTV serum in a micro-Ouchterloney diffusion plate and a line of identity formed. Fluorescent antibody tests showed a specific surface antigen in about 20% of a suspension of cultured tumor cells. MTV antigen was present in the milk of 9/12 C57BL/Haag mice inoc. with tumor extract.

823 STUDIES ON INTERFERON INDUCTION BY THE MOUSE MAMMARY TUMOR VIRUS. (E.) Laing, D. H. (Schering Corp., Bloomfield, N. J.) and D. H. Moore. Proc. Soc. Exp. Biol. Med. 133(1):252-254, 1970.

Milk from female C57BL/Haag and male Swiss mice, i.v. with 0.1 ml mouse mammary tumor virus (MTV; about 10^{10} - 10^{12} particles), milk from lactating mice (containing as much as 10^{12} MTV particles/ml), and conc. medium from the CCL-51/060562 cell line (actively producing MTV) were assayed for interferon by the plaque inhibition test, with negative results. MTV failed to induce resistance in male Swiss mice challenged with Columbia SK virus, and no specific hemagglutinin activity (HA) could be found. It is concluded that although MTV shares certain properties with the myxoviruses, it lacks interferon activity and interferon-inducing capacity.

824 MECHANISM OF PERSISTENT HERPES SIMPLEX VIRUS INFECTION IN VITRO. (E.) Hampar, B. (NCI, Bethesda, Md.) and M. A. K. Burroughs. Nat. Cancer Inst. 43(3):621-634, 1969.

SAE strain of herpes simplex virus (HSV) was adapted by passage in Chinese hamster (MAL) and in cell lines and inoc. into MAL cells. Persistent infection (eventual termination of cytopathic effects and viral synthesis) was characterized by changes in the properties of cells, an increased resistance to HSV; and changes in the virus, an increased virulence for instant cells. The termination of the infection was due to interference with the virus directly or by the production of an intracellular inhibitor. Persistent infection depends on the

genetic properties of the cell and may be related to recurrent herpes infection in humans.

70-825 VIRUS AS THE CAUSE OF RHINOPHARYNGEAL CARCINOMA. (E.) Laing, D. (50 1/3 Gloucester Bldgs., Hong Kong). Acta Otolaryng. (Stockholm) 67(2-3):190-199, 1969.

Serological tests of 47 Hong Kong Chinese pts. with nasopharyngeal carcinoma (NPC) showed a higher frequency of antibodies to adenoviruses 7 and 12 than in the normal Chinese population. Precipitating antibodies to an antigen from Burkitt's lymphoma cells were found in sera from 23/27 Chinese pts. with NPC (85%). In 1956-1961 (inclusive), the NPC incidence in all Chinese, in the "boat people" and in other population groups of Hong Kong, was 78, 124 and 76/million/yr., resp. Studies of the high-risk "floating population" of Hong Kong disclosed no evidence for a vector-borne disease (yellow fever is unknown, reovirus has not been isolated, and the local environmental conditions do not favor the multiplication of mosquitoes) and no evidence of unusual exposure to other environmental factors such as kitchen smoke, opium, snuff or tobacco chewing. The "boat people" of Hong Kong are a highly inbred population (most are Tan Ka, descended from families of mainland Kwangtung), and most of the families have lived in the Hong Kong area for centuries. The possibility of a genetically-determined susceptibility to tumor virus(es) is mentioned, but no conclusions could be drawn.

70-826 RELATION BETWEEN EPSTEIN-BARR VIRAL AND CELL MEMBRANE IMMUNOFLOUORESCENCE IN BURKITT TUMOR CELLS. III. COMPARISON OF BLOCKING OF DIRECT MEMBRANE IMMUNOFLOUORESCENCE AND ANTI-EBV REACTIVITIES OF DIFFERENT SERA. (E.) Klein, G. (Karolinska Inst. Sch. Med., Stockholm), G. Pearson, G. Henle, W. Henle, G. Goldstein and P. Clifford. J. Exp. Med. 129(4):697-705, 1969.

Sera from pts. with Burkitt's lymphoma (BL), infectious mononucleosis (IM) and carcinoma of the postnasal space (CaPNS), showed a good correlation between antibody which blocks direct membrane staining of BL cells by fluorescein isothiocyanate (FITC)-conjugated serum and anti-Epstein-Barr virus (EBV) titers. The IM sera generally had lower activities of both, and CaPNS sera also had a good correlation between low levels of blocking antibody and anti-EBV. In all, 102/279 showed high blocking activity and high anti-EBV; 124/279 showed low levels of both; 22 (8%) showed low anti-EBV and high blocking activity; and 31 (11%) showed a low blocking activity and a high anti-EBV.

70-827 RELATION BETWEEN EPSTEIN-BARR VIRAL AND CELL MEMBRANE IMMUNOFLOUORESCENCE

IN BURKITT TUMOR CELLS. IV. DIFFERENTIATION BETWEEN ANTIBODIES RESPONSIBLE FOR MEMBRANE AND VIRAL IMMUNOFLUORESCENCE. (E.) Pearson, G. (Karolinska Inst. Sch. Med., Stockholm), G. Klein, G. Henle, W. Henle and P. Clifford. J. Exp. Med. 129(4):707-718, 1969.

Sera from 9 relatives of Burkitt's lymphoma (BL) pts. showed low anti-Epstein-Barr virus (EBV) titers and significant indirect membrane immunofluorescence (MIF) reactions; there was also low blocking activity against the fluorescein-conjugated globulin of a BL pt. (F-Mutua), but the MIF and blocking activity were not parallel to each other in 4/9 cases. Sera from one relative (Robert) was conjugated with fluorescein isothiocyanate (FITC) and found to have a similar target cell spectrum as F-Mutua, but it was blocked by sera from several BL pts.; unconjugated Robert serum had no activity against the Mutua conjugate. The MIF titer of Mutua serum absorbed on BL cells was shown to decrease 64-fold while the anti-EBV titer decreased only 3-fold.

70-828 COMPLEMENT-FIXATION TEST FOR DETECTION OF HERPES-LIKE VIRUSES IN CELL CULTURES OF BURKITT'S LYMPHOMA. (E.) McCormick, K. J. (Baylor U. Coll. Med., Houston, Tex.), W. A. Stenback, J. J. Trentin, G. Klein, J. S. Nadkarni, J. J. Nadkarni and P. Clifford. J. Virol. 3(5):525-527, 1969.

Tests for complement-fixing antigen(s) using sera from pts. with Burkitt's lymphoma, pts. with other neoplasms and normal subjects, were negative on 4/4 biopsy specimens of Burkitt's lymphoma, but positive with a number of sera on 4/6 Burkitt cell lines. The degree of complement-fixing reactivity in the Burkitt cell lines was correlated with the ease of detecting herpes-like virus by electron microscopic examination; viral particles were seen exclusively in cell lines with complement-fixing reactivity.

70-829 STUDIES ON THE RELATION OF MEMBRANE IMMUNOFLUORESCENCE TO EPSTEIN-BARR VIRUS INFECTION. (E.) Dunkel, V. C. (NCI, Bethesda, Md.) and R. F. Zeigel. J. Nat. Cancer Inst. 44(1):133-144, 1970.

All sera from pts. with Burkitt's lymphoma (BL) and from normal subjects reacted positively by indirect membrane immunofluorescence and direct immunofluorescence on the EB virus-containing cell lines HRI-K (BL) and 64-10 INF (myeloid leukemia), indicating a direct relationship between viral infection of the cells and membrane reactivity. Only the membranes of virus-producing HRI-K and 64-10 INF cells were covered with antibody, as visualized by electron microscopic examination. The control 64-10 cells (myeloid leukemia) were negative in both immunofluorescent tests. The Raji cell line (BL) was negative

when tested for virus by direct immunofluorescence but small proportions of Raji cells (0.4-2.5%) reacted with 5/18 BL sera by indirect membrane immunofluorescence. Immunofluorescence was observed on the membrane of 64-10 cells following incubation with EB virus; electron microscopic examination demonstrated adsorbed virus, but no layer of antibody, on the cell surface.

70-830 ELECTRON MICROSCOPIC STUDIES ON HERPES-TYPE VIRUS IN A BURKITT LYMPHOMA CELL LINE. (E.) Yamaguchi, J. (Tohoku U. Res. Inst. Tubercul. Leprosy Cancer, Sendai, Japan). Gann Monogr. 7:77-94, 1969.

Electron microscopic examination showed 2 types of EB virus in the P3HR-1 Burkitt lymphoma cell line, naked particles and larger, less numerous enveloped particles. The virus appeared in either intact, altered or, more frequently, degenerated and disintegrated cells. Certain observations suggested that the virus originated and matured in the nucleus and was discharged from the cell by budding or by disruption of the cell. The virus consisted of icosahedral capsids with 162 capsomeres and was clearly a herpes virus. Quantitative electron microscopy indicated a peak virus production of 200 particles/cell and an envelope around only 10% of the particles released into the medium.

70-831 STUDIES ON EB VIRUS OF BURKITT'S LYMPHOBLASTS. (E.) Weinberg, A. (Hebrew U. Hadassah Med. Sch., Jerusalem) and Y. Becker. Virology 39(2):312-321, 1969.

EB3 and GOR cell lines of Burkitt's lymphoblasts containing EB virus were incubated in arginine-depleted Eagle's medium with radiolabeled thymidine, followed by isolation of EB virus particles in sucrose gradients. The EB virus contained radioactive DNA and protein and resembled herpes simplex virus in its electron microscopic appearance, in the sedimentation constant of its DNA and in the protein composition of its coat.

70-832 THE ATTENUATION, WITH LOSS OF ONCOGENICITY, OF THE HERPES-TYPE VIRUS OF MAREK'S DISEASE (STRAIN HPRS-16) ON PASSAGE IN CELL CULTURE. (E.) Churchill, A. E. (Houghton Poultry Res. Station, England), R. C. Chubb and W. Baxendale. J. Gen. Virol. 4(4):557-564, 1969.

During continuous passage of Marek's disease virus (strain HPRS-16) in chicken kidney cell cultures, the plaque size and the rate of development of cytopathic effects increased, accompanied by a loss of viral pathogenicity in newly hatched Rhode Island Red chicks by passage 33 *in vitro*. The major viral antigen, detected by gel diffusion of cell extract and

ture fluid, became weaker after passage 20 disappeared by passage 30. The virus late lacking this antigen was of little or no antigenicity in live chickens and did not interfere with the pathogenicity in vivo or in vitro of virus containing this antigen.

833 THE IN VITRO TRANSFORMATION BY AN AVIAN ADENOVIRUS (CELO). III. HUMAN TUMOR CELL CULTURES. (E.) Anderson, J. Baylor U. Coll. Med., Houston, Tex.), V. J. Anderson, V. Jasty and L. O. Mancini. J. Nat. Cancer Inst. 43(3):575-580, 1969.

Human amnion cells were inoc. (10^9 embryo lethal dose 50/ml) with chicken-embryo-lethal-orphan virus (CELO). Earliest signs of cellular change were apparent on the 21st day - pleomorphic cells, nuclei of varying size with frequent pairing. In culture every 3 days established 3 lines which, at the third passage, were stellate with abundant cytoplasm, and eventually assumed a spindle-shaped morphology. Fluorescent antibody studies of the three lines revealed intranuclear CELO-specific T antigen which appeared to be identical to that in CELO-transformed hamster cells. Mice inoc. in the cheek pouch with 6.5×10^6 cells developed tumors in three days; 10^6 cells from the 15, 20, and 30 passages caused tumor development in two weeks. After histologic examination, the tumors were identified as fibrosarcomas.

834 VIROLOGIC-IMMUNOLOGIC FINDINGS IN TUMOR PATIENTS. (Ger.) Tauchnitz, C. (Univ. Med. Clin., Leipzig, Germany), H.-P. Tauchnitz and E. Luschnitz. Z. Immunitaetsforsch. 125(5):382-389, 1969.

Sera from 170 pts. with malignant tumors but without detectable metastases (37 bronchial carcinoma (Ca), 40 breast Ca, 22 cervix or corpus uteri Ca, 25 with different sarcomas, 46 with different Ca) were tested for the presence of adenovirus-18 neutralizing antibodies and results compared to those from healthy subjects. Antibodies were significantly less frequent in cancer pts. than among normal subjects: at a 1:10 dilution, the sera contained neutralizing antibodies in 27.1% of the tumor pts. and 41.5% of the controls; at 1:5 dilution the frequency was 45.9% and 69.3%, resp. (in 101 controls). Differences were significant for bronchial carcinoma (24.3% at 1:10 and 32.4% at 1:5 dilution), for breast Ca (22.5% and 47.5%, resp.), for genital carcinoma (9.1% and 31.8%, resp.), and for different sarcomas (20.0% and 44.0%, resp.), but not for different Ca (45.7% and 63.0%, resp.). Analysis revealed that the more frequent presence of neutralizing antibodies in the mixed carcinoma group was not accompanied by a more benign course of disease (36.9% of fatal cases and 13.1% of metastases over a 9-18-mo. observation period, compared to 27.4% and 10.5%, resp., in

the other groups). In additional experiments with 143 sera no difference in hemagglutination tests against parainfluenza virus 1 was observed between these different groups.

70-835 MECHANISM OF VIRAL CARCINOGENESIS BY DNA MAMMALIAN VIRUSES, VII. VIRAL GENES TRANSCRIBED IN ADENOVIRUS TYPE 2 INFECTED AND TRANSFORMED CELLS. (E.) Fujinaga, K. (Aichi Cancer Ctr., Nagoya, Japan) and M. Green. Proc. Nat. Acad. Sci. USA 65(2):375-382, 1970.

In DNA-RNA hybridization inhibition and hybridization competition experiments, the virus-specific RNA sequences synthesized during productive infection of KB cells with human adenovirus type 2 (Ad 2) were compared with those synthesized in virus-free Ad 2-transformed rat embryo cells. At 6 hours after infection of KB cells, the early RNA represented 8-20% of the viral genome. All early viral RNA sequences were also detected at 18 hr. after infection (in early plus late RNA). The RNA sequences in transformed cells corresponded to 50% of early RNA sequences in infected cells but to none of the late RNA sequences. The results indicate that only 4-10% of the viral genome is transcribed in Ad 2-transformed cells.

70-836 ALTERED PROPERTIES OF THYMIDINE KINASE INDUCED IN HAMSTER KIDNEY CELLS BY ADENOVIRUS TYPES 5 AND 12. (E.) Ogino, T. (Osaka U. Res. Inst. Microbiol. Dis., Japan) and M. Takahashi. Biken J. 12(1):17-23, 1969.

Deoxythymidine kinase (TdR kinase) activity in adult hamster kidney cells increased 10-30-fold over control values after infection with adenovirus Type 5 (AV-5) and 2-4-fold in cells infected with adenovirus Type 12 (AV-12). TdR kinase of AV-5-infected cells was much more heat-labile (at 40° C) and TdR kinase from AV-12-infected cells was slightly more heat-labile, than TdR kinase from uninfected cells. TdR kinases from cells infected by either AV-5 or AV-12 showed a 3-4-fold increase in the Michaelis constants. Studies in infected cells exposed to puromycin or cytosine arabinoside indicated that the enhanced TdR kinase activity required de novo protein synthesis, but not DNA synthesis. Extracts of AV-5- or AV-12-infected cells did not activate the TdR kinase of extracts from uninfected cells; extracts from uninfected cells were similarly inactive with respect to TdR kinase from infected cells. It is concluded that infection of hamster kidney cells with AV-5 or AV-12 induced a new species of TdR kinase.

70-837 INDUCTION OF CELLULAR DNA SYNTHESIS BY ADENOVIRUS 12 IN HUMAN EMBRYO KIDNEY CELLS. (E.) Yamashita, T. (Nat. Inst. Health, Tokyo) and H. Shimojo. Virology 38(2):351-355, 1969.

Non-growing human embryo kidney cells were infected with adenovirus 12 strain Huie and pulse-labeled with ^3H -thymidine. The virus replicated efficiently. At high infectious doses, DNA synthesis increased after 16 hour, reaching a max. in 24-28 hour.; a lower, but definite synthesis was induced with lower infectious doses. DNA synthesis was not induced when the virus was neutralized with anti-adenovirus 12 rabbit serum. Hybridization studies of the induced DNA showed some homology with cellular DNA early in the viral replication cycle; but after 24 hr., the major part of the DNA was viral.

- 70-838 PURIFICATION AND ANALYSIS OF ADENOVIRUS GROUP-SPECIFIC 'T' ANTIGEN. (E.) Hollinshead, A. (George Washington U. Lab. Virus Cancer Res., Washington, D. C.), B. Bunnag, T. Alford and C. Cusumano. J. Gen. Virol. 4(3):433-435, 1969.

On vertical disk-gel electrophoresis, a partially purified preparation of adenovirus type 12 group-specific T antigen yielded 3 protein bands which reacted in complement-fixation tests using serum from tumor-bearing hamsters. An N-terminal amino acid analysis demonstrated alanine and leucine end groups in one of the proteins, alanine and isoleucine end groups in the second, and alanine alone in the third. Removal of 80% of the lipid from the partially purified T antigen, leaving some phospholipid behind, rendered the specimen heat-labile, but still reactive in complement fixation tests. Removal of 90% of the lipid, including all phospholipid detectable by thin-layer chromatography, abolished complement-fixing reactivity.

- 70-839 CYTOCHEMICAL OBSERVATIONS ON THE ADENOVIRUS TYPE-12-TRANSFORMED HAMSTER-EMBRYO CELL CULTURES. (E.) Malinin, G. I. (Biomed. Res. Inst., Rockville, Md.). J. Nat. Cancer Inst. 43(3):693-717, 1969.

Uninfected, pooled, hamster embryo cells were grown as confluent monolayers and classified into 3 types morphologically and cytochemically. Up to 5 days after inoc. with adenovirus type 12 (strain Huie), no change was noted; at about 7 days, types 2 and 3 showed some nuclear disintegration and deposition of nuclear particles extracellularly throughout the monolayer - some DNA-protein also penetrated into cells. Stellate or globular perinuclear cytoplasmic inclusions were seen which stained intensely for RNA, and hexagonal crystals, containing DNA were also seen, mainly extracellularly, but also within the cytoplasm and nucleus of some cells. After another 6-10 days the formation of giant cells and transformed colonies became evident. Surviving type 2 and 3 cells changed to multi-layered round or ovoid colonies and had strong staining reactions for proteins, tyrosine, DNA,

but not for RNA. Type 1 transformed simultaneously, but independently of types 2 and 3, forming giant cells marked by a decrease of nucleocytoplasmic ratio. Cells not involved in transformation developed large cytoplasmic granules and a chromophobic Golgi zone. It is believed that high levels of RNA and proteins are necessary for transformation by adenovirus type 12, and that DNA and proteins are essential for growth.

- 70-840 INFLUENCE OF SYNTHETIC (POLY I:C) AND VIRAL DOUBLE-STRANDED RIBONUCLEIC ACIDS ON ADENOVIRUS 12 ONCOGENESIS IN HAMSTERS. (E.) Larson, V. M. (Merck Inst. Ther. Res., West Point, Pa.), W. R. Clark and M. R. Hilleman. Proc. Soc. Exp. Biol. Med. 131(3):1002-1011, 1969.

Newborn random-bred golden Syrian hamsters were inj. s.c. with 0.2 ml of adenovirus 12; drug or phosphate-buffered saline was given i.p. in 0.1 ml vol. at various dosage schedules. When the drug was polyriboinosinic (poly I) or polyribocytidylic (poly C) acid, given individually or complexed (poly I:C), there was no difference between treated and control hamsters with respect to development of s.c. tumors, but up to 44% protection against internal tumors, poly C being effective only in females. The effects of multiple doses of interferon inducers before and after inj. with adenovirus 12 were: no effect on s.c. tumors; poly I:C and coliphage MU6-RNA were highly active in preventing internal tumors, especially in females; pyran and endotoxin had lesser effects.

- 70-841 INFLUENCE OF SYNTHETIC DOUBLE-STRANDED RIBONUCLEIC ACID, POLY I:C, ON FRIEND LEUKEMIA IN MICE. (E.) Larson, V. M. (Merck Inst. Ther. Res., West Point, Pa.), W. R. Clark, G. E. Dagle and M. R. Hilleman. Proc. Soc. Exp. Biol. Med. 132(2):602-607, 1969.

Male BALB/c mice, 4-6 weeks old, were given 0.2 ml Friend leukemia virus (FLV) i.p., and a synthetic complex of polyriboinosinic and polyribocytidylic acid (poly I:C) at various dosage schedules. The effects of (poly I:C) were: a single dose given 6 hour before virus increased the degree of splenomegaly, but had a beneficial effect when the amount of drug was reduced to 4 ug; treatment before and after FLV temporarily reduced spleen wt., but eventually resulted in larger spleens and earlier deaths; initiation of treatment after virus inoculation was associated with reduced splenomegaly (also reduced necrosis and hemorrhage) and a longer survival. All 3 schedules temporarily reduced virus titer in plasma by 10 days. Cortisone admin. prior to FLV, alone and in combination with (poly I:C), greatly increased the splenomegaly.

-842 INFLUENCE OF SYNTHETIC DOUBLE-STRANDED RIBONUCLEIC ACID (POLY I:C) ON SV40 TUMOR ONCOGENESIS AND TRANSPLANT TUMOR IN HAMSTERS. (E.) Larson, V. M. (Merck Inst. Ther. Res., West Point, Pa.), P. N. Panteleakis and R. Hilleman. Proc. Soc. Exp. Biol. Med. 132(1):14-19, 1970.

The time of inoc. and the number of doses of polyribonucleic:polyribocytidylic acid complex (poly I:C) i.p. had no effect on the development of s.c. tumors in adult male golden Syrian hamsters given s.c. inj. with 1×10^3 - 5×10^5 tumor cells (F5-1 line). The only effect of viral oncogenesis in newborn hamsters was a slight delay (14-21 days) in detection of early tumors in animals given poly I:C before virus.

-843 INHIBITORY EFFECT OF A SYNTHETIC INTERFERON INDUCER ON MURINE SARCOMA AND LEUKAEMIA VIRUS INFECTION IN VITRO. (E.) Barma, P. S. (NIH, Bethesda, Md.), S. Baron, R. J. Ebner and G. Shiu. Nature (London) 224(5219):4-605, 1969.

The synthetic RNA, polyinosinic:polycytidylic acid (100 µg/ml, beginning 18 hours before viral infection) inhibited viral replication and transformation in mouse embryo fibroblasts infected with mouse sarcoma virus or Rauscher, Friend, or Gross mouse leukemia viruses.

-844 TRANSFORMATION OF HAMSTER EMBRYO CELLS AND TUMOR INDUCTION IN NEWBORN HAMSTERS BY SIMIAN ADENOVIRUS SV11. (E.) Busto, B. C. (Inst. Biomed. Res. Education Res. Fund., Chicago, Ill.). J. Virol. 3(5):513-519, 1969.

Simian adenovirus SV11 produced foci of transformed hamster embryo cells which were unusual for adenoviruses, appearing as early as 7 days after inoc. and usually consisting of small, rounded, loosely adhered cells (often with multilobed or multiple nuclei) which upon in vitro passage grew separately or formed small clusters or chains. With less than 2.8 PFU/cell, focus formation was linearly related to virus dilution; with 5.6 PFU, no focus formation was observed. The av. PFU/FFU ratio was relatively low (3.8×10^4). The transformed cells contained complement-fixing antigen in tests using serum from tumor-bearing hamsters. The s.c. inoc. of transformed cells into 1-week-old hamsters induced tumors in 8/8 within 3 weeks. 7/10 newborn hamsters and 5/12 3-day-old hamsters, s.c. inoc. of SV11 induced tumors within 91 and 122 days, resp.

-845 INDUCTION OF TUMOR-SPECIFIC TRANSPLANTATION IMMUNITY IN HAMSTERS WITH CELL FRACTIONS FROM ADENOVIRUS AND SV40 TUMOR CELLS. (E.) Coggin, J. H. (U. Tennessee,

Knoxville), L. H. Elrod, K. R. Ambrose and N. G. Anderson. Proc. Soc. Exp. Biol. Med. 132(1):328-336, 1969.

Weanling golden Syrian hamsters were immunized (3 inj./week of 1.0 ml i.p.) with either X-irradiated adenovirus 31 tumor cells (5×10^6 cells/ml), tumor cell homogenate, or fractions of the homogenate separated by differential centrifugation. The hamsters were then challenged (10-14 days after the third immunization) with 4 or 8×10^6 homologous tumor cells. The crude membrane fraction stimulated transplantation immunity comparable to that induced by irradiated whole cells; the other fractions were not as effective, and the tumor cell homogenate gave no protection. In a similar experiment, mature hamsters were immunized with SV40 virus (strain VA45-54), whole X-irradiated tumor cells (F5-1 line), frozen and thawed tumor cells, or tumor cell ghosts. The cell ghosts gave the same absolute protection against challenge with homologous tumor cells as did the virus or irradiated cells, but unlike them, the cell ghosts had no oncogenic potential. The frozen and thawed cells were ineffective.

70-846 ENHANCED VIRUS TRANSFORMATION OF HAMSTER EMBRYO CELLS IN VITRO. (E.) Coggin, J. H., Jr. (U. Tennessee, Knoxville). J. Virol. 3(5):458-462, 1969.

Aging of hamster embryo cells (HEC) in vitro (up to 87 days) increased their susceptibility to transformation by SV40. Pretreatment with x-irradiation (150 r) or with 5-iodo-2'-deoxyuridine also sensitized HEC to SV40-induced transformation, the transformation efficiency being increased more than 50- and 25-fold, resp. A 10-hr. delay between irradiation and the addition of virus reduced the increased susceptibility of irradiated HEC. Irradiation increased HEC sensitivity to transformation by adenovirus 31 as well as SV40.

70-847 NUTRITIONAL VARIATION INFLUENCE ON SIMIAN VIRUS 40-TRANSFORMED HUMAN AMNION CELL STRAINS. (E.) Fogh, J. (Sloan-Kettering Inst. Cancer Res., New York, N. Y.) and E. V. Gaffney. J. Nat. Cancer Inst. 44(1):215-223, 1970.

The influences of McCoy's medium and medium 512, each supplemented with either agamma calf serum or fetal bovine serum, on SV40-transformed human amnion cells were compared. The growth potential, in terms of transfer dilutions or culture longevity before crisis, was greater in McCoy's medium than in medium 512, was increased by the presence of agamma calf serum in both media, and was not altered by changing the medium or serum during subcultivation. The cell morphology, reversible by changing the medium, was epithelial-like in McCoy's medium and fibroblastic

in medium 512. Chromosomal alterations were observed in all combinations of serum and media. Virus production was rather constant in medium 512 with fetal bovine serum, but triphasic in the remaining combinations of medium and serum. The amount and time of appearance of T and V antigens varied with the medium and serum, the antigens appearing earliest with McCoy's medium supplemented by either serum.

70-848 NEW ANTIGENS IN CELLS TRANSFORMED BY SV40. I. DEMONSTRATION OF THREE NEW ANTIGENS IN SEVERAL CELL LINES OF DIFFERING ORIGIN, FOLLOWING TRANSFORMATION BY SV40. (Fr.) de Vaux Saint Cyr, C. (Inst. Sci. Res. Cancer, Villejuif, France), A. Herbet, E. Sobczak, R. Wicker and P. Grabar. Int. J. Cancer 4(5): 616-625, 1969.

The presence of 3 hitherto-undetected antigens was demonstrated by immunoelectrophoretic studies using rabbit and hamster antisera against a cell line derived from a tumor induced in a neonatal Syrian hamster by SV40 and a number of cell lines transformed *in vitro* by SV40 (hamster embryo cells, kidney cells of MKS-Bu 100 mice, rat fibroblasts, dog kidney cells and kidney cells of a Rhesus monkey). These newly-demonstrated antigens were not formed by cell lines of hamster embryo fibroblasts undergoing spontaneous transformation *in vitro*, nontransformed hamster embryo fibroblasts, BHK cells, or cells derived from hamster tumors induced by polyoma virus or adenovirus-12. Tentatively designated A, B and C, their fluorescent localization and absorption studies with a purified preparation of T antigen confirmed that they were different from T antigen and probably different from the so-called transplantation antigen.

70-849 ULTRASTRUCTURAL LOCALIZATION OF SV40 T ANTIGEN WITH ENZYME-LABELLED ANTIBODY. (E.) Leduc, E. H. (Brown U., Providence, R. I.), R. Wicker, S. Avrameas and W. Bernhard. J. Gen. Virol. 4(4):609-614, 1969.

SV40-infected MA 104 monkey kidney cells were treated with unlabeled hamster antiserum against the T antigen, followed by peroxidase-labeled rabbit antiserum against hamster immunoglobulin, and examined by electron microscopy. In uninfected cells, an electron-dense reaction product of peroxidase was observed either in all cytoplasmic elements of some cells in a given specimen or as a thin layer on the surface of all cells. In some infected cells, heavy staining was distributed uniformly throughout the nucleoplasm except the nucleolus, while in other infected cells the T antigen appeared as a reticular network throughout the nucleus, again excluding the nucleolus.

70-850 ANTIGENIC CHARACTERISTICS OF TUMORS INDUCED IN SYRIAN HAMSTERS BY SIMIAN

VIRUS 40. (E.) Kaliev, Y. (Inst. Exp. Clin. Oncol., Moscow). Neoplasma (Bratisl.) 16(3): 285-291, 1969.

The duration of the latent period of 20 primary SV40-induced tumors in golden hamsters did not significantly affect the immunosensitivity of the primary tumors in immunized, isologous hosts. The immunosensitivity of the tumors was not correlated with their immunogenicity in inducing immune resistance to transplantation of a standard tumor in isologous, normal, adult hamsters, and individual hamsters differed in their immunological reactivity under these conditions.

70-851 HUMAN DIPLOID CELL TRANSFORMATION BY DNA EXTRACTED FROM THE TUMOR VIRUS SV40. (E.) Aaronson, S. A. (NCI, Bethesda, Md.) and G. J. Todaro. Science 166(3903):390-392 1969.

In normal human fibroblasts (F.R. strain) infected with DNA from small-plaque SV40, transformed colonies typical of SV40 transformation appeared 2-3 weeks after infection. Several clones of transformed cells were propagated. All of these clones contained SV40 T antigen, and yielded infectious SV40 after cocultivation with green monkey kidney cells in the presence of UV-inactivated Sendai virus. Evidence is presented to show that a single molecule of SV40 DNA was sufficient to transform these cells permanently and to induce SV40 T antigen.

70-852 HETEROKARYON FORMATION OF SIMIAN VIRUS 40-TRANSFORMED CELLS IN THE PRESENCE OF ULTRAVIOLET-IRRADIATED SENDAI VIRUS. (E.) Dubbs, D. R. (Baylor U. Coll. Med., Houston, Tex.) and S. Kit. J. Virol. 3(5):536-538, 1969.

Mouse kidney cell lines transformed by UV-irradiated SV40 (mKS-U cell lines), with nuclei labeled by ³H-thymidine, were fused with CV-1 green monkey kidney cells in the presence of UV-irradiated Sendai virus (UV-SV). In the presence of UV-SV, 3/3 cell lines showing good SV40 yield, 3/3 av. yielders, 4/4 rare yielders, 2/2 poor yielders and 12/14 non-yielders fused with the CV-1 cells, as shown by the appearance of 31-over 70% of the labeled nuclei in the heterokaryons. Under these conditions, SV40 was recovered from mixtures including all of the good, av. and poor SV40-yielding cell lines and from 1/4 of the rare yielders (mKS-U16). No SV40 was rescued from any of the mixtures of CV-1 cells and non-yielding mKS-U cell lines. It is concluded that failure to rescue SV40 from non-yielder mKS-U cells cannot be explained by their failure to fuse with CV-1 cells.

70-853 SYNTHESIS OF A "REPRESSOR" OF SV40 VIRUS IN PRODUCTIVE AND ABORTIVE INFECTION. (Fr.) Cassingena, R. (Inst. Cancer

. Virol. Lab., Villejuif, France), P. rnier, E. May, S. Estrade and M.-F. Bourali. R. Soc. Biol. (Paris) 268(23):2834-2837, 1969.

multiplication of SV40 in cultures of a line cerpopithecus monkey kidney cells (BSC-1) was bited by the addition of an extract of EHSVi ls (a line of Syrian hamster embryo cells nsformed in vitro by SV40) plus a basic polymer ch increased cellular permeability. Such ibition was greater in the presence of poly-rnithine than it was in the presence of poly-or poly-D-lysine. The quantity of repressor nt produced within the first 18 hr. after ection in cultures of both permissive cell es (BSC-1; MA-104, a line derived from rhesus key kidney) and non-permissive cell lines , secondary C3H mouse embryo cells; EH, ndary Syrian hamster embryo cells), appeared e directly proportional to the multiplicity nfection at least up to a multiplicity of 40 /cell, the highest conc. studied. The fact t the repressor was synthesized after abortive ection of mouse and hamster cell cultures gested that it might be a protein involved in ransmission of viral information. The fact t it was demonstrable earlier in these non- missive cultures (by hour 12, as contrasted 18 hours after infection), with a total conc. the end of 24 hours which was 1.5-2.5-fold ater than the conc. found in permissive cell tures, suggested that some constitutional tor in the cells of permissive cultures tended block the repressor and favor expression of viral genome in its entirety.

854 PRESENCE OF A SPECIFIC "REPRESSOR" IN HAMSTER OR RAT CELLS TRANSFORMED BY POLYOMA VIRUS. (Fr.) Zamfiresco, M. (Sci. Res. t. Cancer Virol. Lab., Villejuif, France). R. Acad. Sci. [D] (Paris) 270(17):2139-2141, 1970.

extract of the T.PyXV cell line, derived from polyoma virus (PV; Rowe strain)-induced hamster or, and an extract from a PV-transformed rat ryo cell line, significantly inhibited PV tiplication in a secondary culture of C3H se embryo cells (ES). Extracts from SV40- nsformed hamster embryo cells or from un- ated ES cells, did not have this effect. The ract from T.PyXV cells did not inhibit SV40 tiplication in monkey cells. The inhibitory ct of this specific "repressor" substance nsitive to temperature and trypsin, and ntant to DNase and RNase.

55 DISSOCIATION OF MULTIPLE POLYOMA VIRUS FUNCTIONS BY ULTRAVIOLET IRRADIATION. Herberman, R. B. (NCI, Bethesda, Md.) and . Ting. Proc. Soc. Exp. Biol. Med. 131(2): 464, 1969.

radiation of polyoma virus (PyD) for 10 markedly decreased the infectivity (in

mouse embryo cells), decreased the tumorigenicity and prolonged the latent period for tumor appearance (in golden Syrian hamsters), and reduced the ability to induce hemagglutination-inhibiting (HI) antibodies (mice). After 30 min. of irradiation, the infectivity, tumor incidence, and induced level of HI antibody were insignifi- cant. Pretreatment of C3H mice with virus irradiated for 10 min. induced transplantation resistance similar to unirradiated virus, and the virus which had received a 30-min. UV dose gave much weaker protection; similar pretreatment of C57Bl mice resulted in an increased incidence of tumor growth, especially with the longer irradiated virus.

70-856 NEW DATA ON THE INFLUENCE OF ULTRA- VIOLET IRRADIATION OF POLYOMA VIRUS ON THE TRANSPLANTATION ANTIGEN. (Fr.) Meyer, G. (Regional Cancer Ctr., Marseille, France), J. Fondarai and H. Bonneau. C. R. Soc. Biol. (Paris) 162(12):2171-2173, 1969.

In an effort to replicate the results of a previously reported study, 3 groups of hamsters of an unspecified strain were inoc. with 10^5 or 10^6 PFU of untreated polyoma virus derived from a transplantable CT 54 tumor, or with 10^6 PFU polyoma virus from the same source irradiated with UV (30,000 ergs/mm²). One mo. later, sub- groups of animals in each treatment group were inoc. with cells from the CT 54 tumor in doses representing 15 x, 150 x, and 1500 x the standard TD₅₀. A statistical analysis of tumor takes and latent periods in each of the subgroups confirmed that the protection afforded by the irradiated virus was equivalent to reducing the tumorigenic dose to 10% that in the absence of such irradiation, as previously reported.

70-857 ELECTRON MICROSCOPIC STUDY OF THE FIRST STAGES OF THE INFECTION OF MONKEY (Rhesus resus) KIDNEY CELLS BY SV40 VIRUS IRRADIATED BY ULTRAVIOLET OR GAMMA RAYS. (Fr.) Ferreira-Salgado, M.-A. (Rio de Janeiro Fed. U., Brazil). Bull. Cancer (Paris) 55(3):399-412, 1968.

Cultures of MA 104 cells, derived from rhesus monkey kidney, were incubated for 2 hours at 37° C with culture medium alone, untreated SV40 virus, SV40 virus previously irradiated with UV, or SV40 virus previously irradiated with gamma rays. Electron microscopic studies were made of cells from each group of cultures, 3 and 48 hours after infection, with additional studies of the UV-irradiated and untreated virus cultures made 5 hour after infection. No significant differences between infected cultures were found, as concerned viral adsorption onto the cellular membrane or subsequent viral penetration into the nucleus. However, both groups of cul- tures infected with irradiated virus showed little or no evidence of intranuclear viral replication, although the percentage of cells showing one or more hypertrophied nucleoli was

the same as that found in cultures infected with untreated virus, and significantly higher than that found in non-infected control cultures, confirming the presence of a strong intracellular reaction to the presence of the irradiated virus.

- 70-858 THE FORMATION OF VARIANTS WITH A REVERSION OF PROPERTIES OF TRANSFORMED CELLS. I. VARIANTS FROM POLYOMA-TRANSFORMED CELLS GROWN IN VIVO. (E.) Rabinowitz, Z. (Weizmann Inst. Sci., Rehovot, Israel) and L. Sachs. Virology 38(2):336-342, 1969.

Hamster embryo cells, transformed by polyoma virus (PV), inoc. s.c. into 6-week-old hamsters, produced tumors histologically similar to variants formed in vitro, which differed from the original transformed cells in morphology, and in the fact that they could form colonies on glutaraldehyde-fixed normal cells; had a decreased cloning efficiency in fluid medium or soft agar; failed to multiply at 41° C and retained contact inhibition between both themselves and their parent cells. Both in vivo and in vitro variants had PV-induced nuclear tumor (T) antigen, and the in vivo variant had a higher degree of tumorigenicity than the parent cells.

- 70-859 THE FORMATION OF VARIANTS WITH A REVERSION OF PROPERTIES OF TRANSFORMED CELLS. II. IN VITRO FORMATION OF VARIANTS FROM POLYOMA-TRANSFORMED CELLS. (E.) Rabinowitz, Z. (Weizmann Inst. Sci., Rehovot, Israel) and L. Sachs. Virology 38(2):343-346, 1969.

Polyoma virus (PV)-transformed hamster embryo cells were subcultured every 2-3 days in Eagle's medium by seeding 5×10^5 cells 50 mm dish. After an initial decrease at 14 days, a continued increase in the percentage of variant colonies was seen, identified by their ability to form colonies on glutaraldehyde-fixed normal hamster cells. Subculture at different cell densities (2×10^4 , 2×10^5 or 2×10^6) indicated that subculture at the lowest density gave the highest frequency of variants.

- 70-860 ALKALINE DEGRADATION OF POLYOMA VIRUS. (E.) Perry, J. L. (Kansas State U., Manhattan), C. M. To and R. A. Consigli. J. Gen. Virol. 4(3):403-411, 1969.

The effects of a carbonate-bicarbonate buffer (a pH 10.5 buffer was used throughout) on purified wild-type polyoma virus (PV) particles were studied. Exposure to buffer at relatively low ionic strengths resulted in degradation of the PV particles, but degradation was less when the buffer conc. was 0.3-0.5 M. The degradation products were separated by density gradient centrifugation and studied by infectivity, hemagglutination assays and electron microscopic examination. The stages of degradation caused

by the buffer depended on the ionic strength of the buffer soln. The PV particles were swollen after exposure to 0.05 M buffer; this swollen state also permitted penetration by DNase. Exposure to 0.1 M buffer resulted in a release of viral DNA from the PV coat. Some PV particles were completely degraded into individual capsomeres after exposure to the buffer (even at 0.05 M). Hemagglutinating (HA) activity was reduced by exposure to 0.05 M buffer, and this activity was zero after exposure to 0.2 M buffer. As the ionic strength of the buffer was increased past 0.2 M, however, some HA activity remained, indicating protection from vigorous degradation.

- 70-861 HETEROGENEITY OF POLYOMA VIRUS DNA: ISOLATION AND CHARACTERIZATION OF NON-INFECTIOUS SMALL SUPERCOILED MOLECULES. (E.) Blackstein, M. E. (U. Toronto, Canada), C. P. Stanners and A. J. Farmilo. J. Molec. Biol. 42(2):301-313, 1969.

Strains of polyoma virus, each derived from a single plaque isolate, were passaged serially in mouse embryo cells using a high multiplicity of infection. Lysates from successive passages contained increasing amounts of either of 2 supercoiled, circular DNA molecules, which were 75% and 50% of the molecular wt. of the major DNA component and lacked infectivity. It is suggested that these 2 new classes of DNA represent deletion mutants of the virus.

- 70-862 RAMBOURG'S TECHNIQUE USED TO DEMONSTRATE THE PRESENCE OF GLYCOPROTEINS IN A CELL STRAIN TRANSFORMED BY POLYOMA VIRUS: ASPECTS OF CELLULAR DIFFERENTIATION. (Fr.) Cesarini, J. P. (Regional Ctr. Cancer, Marseille, France) and H. Bonneau. C. R. Soc. Biol. (Paris) 162(12):2168-2171, 1969.

In an electron microscopic study of thin tissue segments from passages 5 through 7 of transplantable sarcomas induced by polyoma virus in hamsters of an unspecified strain, the application of phosphotungstic acid of low pH made it possible to distinguish a zone rich in collagen, with cells completely surrounded by mucopolysaccharides, made up of normal fibroblasts arising from the stroma and showing no discernible anomalies of the nucleus, cytoplasm, or overall morphology. Other zones, which were less rich in collagen and mucopolysaccharides, were made up of malignant cells which could be readily distinguished by the organization of glycoproteins in the intercellular spaces. The material colored by phosphotungstic acid could not be superposed on the ergastoplasm (which was often reduced to a few, thin layers and sometimes much dilated) but was present in high conc. in the extracellular spaces. At the heart of a tumor, some of these zones were very rich in such material, with cells clearly separated from one another and completely surrounded by a layer

the material in question, whose thickness varied from 1-5 microns. In other zones, which were less rich in the contrast material, the cells were directly in contact with one another. The contrast material was found in the form of small points, which were distributed over the surface of the cell. Similar studies of tissue cultures derived from the same tumors were considerably less productive. Normal elements arising from the stroma were completely absent. Intracellular mucopolysaccharides were much increased, probably because of retention resulting from the clumping together of the transformed cells.

63 EFFECT OF A MOUSE KIDNEY PASSAGE ON THE ONCOGENIC POTENCY OF A POLYOMA VIRUS. (It.) Cassai, E. (U. Ferrara Inst. Biol., Italy) and M. Terni. Boll. Ist. Super. milan. 48(2):97-107, 1969.

Polyoma virus (prepared by inoc. of polyoma virus 210-22 into secondary cultures of mouse embryo cells *in vitro*) was inoc. s.c. into a born Swiss mouse, and a virus (RTT) was isolated subsequently from a culture of the embryonic cells of the infected animal. When inoc. into newborn Swiss mice, golden hamsters and inbred rabbits, both CET and RTT showed essentially the same hemagglutination characteristics (in terms of being active or inactive at different pH's and temperatures), the same plaque morphology, and the same oncogenic potency (in terms of the number of animals showing tumor takes at different dose levels). However, both the infective and the hemagglutinating activities of the virus were significantly greater, as was its frequency of induction of cardiac, mediastinal, renal, and multiple tumors in the treated animals.

54 INTERSTRAIN RESISTANCE TO POLYOMA VIRUS ONCOGENESIS AND RUNTING IN INbred MICE TREATED WITH ANTILYMPHOCYTE SERUM. (E.) Al-Falluji, M. (Ohio State U., Columbus), J. P. Minton, and M. C. Dodd. Proc. Exp. Biol. Med. 132(1):136-141, 1969.

DBA/2 (polyoma tumor resistant) and DBA/2 (polyoma tumor susceptible) mice were inj. s.c. various times with the LID-1 strain of polyoma virus (PV) - 0.05 ml containing 5 hemagglutinating units, and 0.1 ml i.p. antilymphocyte serum (ALS) from female, New Zealand, white mice hyperimmunized with mouse spleen cells. In DBA/2 mice, inj. of PV and ALS during the first week of life resulted in runting and a high mortality; given within the first 2 weeks, developed parotid gland tumors by week 19. The incidence of tumors was related to the time of inj. of PV, and tumor production, early mortality and runting were associated with the developmental age of the animals. In C57BL/6J mice, tumors were not developed if a combined inj. was given during

the first 3 days of life, and mild runting if inj. within the first week.

70-865 ONCOGENESIS OF POLYOMA VIRUS AND IMMUNE RESPONSE PRODUCING ANTIBODIES. (It.) Pitzurra, M. (State U. Perugia Inst. Hyg., Italy) and A. M. Iorio. Ann. Sclavo 11(1):36-52, 1969.

In newborn golden hamsters and Swiss white mice, as in adult animals and animals only a few days old, all inoc. i.p. with polyoma virus of the LID-1 VR 252 strain, there was no demonstrable correlation between the extent of tumor development and the level of antibodies inhibiting hemagglutination of the virus (AIH). The AIH titer was higher in newborn animals than it was in adults, and higher in hamsters than it was in mice. There was no correlation between the AIH titer and the size of the virus dose admin. In hamsters inoc. i.p. with the virus as above, as in hamsters inoc. s.c. with cells from a s.c. fibroma developed in a hamster treated with the virus at birth, complement fixation antibodies against the soluble tumor antigens developed progressively as tumor growth progressed. AIH were lacking entirely in the animals bearing s.c. transplanted tumor cells; none of these transplants were rejected. It is concluded that multiplication of the polyoma virus can lead to cellular transformation *in vivo* by means of a process of DNA hybridization, which is not influenced by the immune response but only by the condition of the genome of the individual host cell.

70-866 GROWTH OF RENAL SARCOMAS INDUCED BY POLYOMA VIRUS. (Ger.) Prechtel, K. (U. Munich Path. Inst., Germany), H. Zobl, L. Herzog and A. Georgii. Verh. Deutsch. Ges. Path. 52:408-410, 1968.

A 16-18-day latent period was seen between perinatal infection of Wistar rats with polyoma virus and microscopic manifestations of tumor. The tumor vol., number of multicentric sarcoma nodules and the latent period were virus dose-dependent. The median generation time of the tumor cells was 28-33 hours (autoradiographic determinations). In attempts to elucidate the question of unicellular or multicellular origin of the sarcoma nodules, approx. 1000 newborn rats were infected with 4 different virus dilutions and the kidneys were examined histometrically 20-50 days later. Results on the one hand seemed to support the hypothesis of unicellular (monoclonal) origin (sufficiently short generation time and virus dose-independent tumor size); on the other hand, however, other data indicated a pluricellular (pluriclonal) composition of the nodule (significant pause in growth between neoplastic transformation and tumor manifestation, whereby the delayed tumor manifestation after

low dilution of virus can only be explained by the existence of pluricellular malignant transformation of cell groups.

- 70-867 INDUCTION OF FIBROSARCOMAS IN RABBITS BY POLYOMA VIRUS. (E.) Lehman, J. M. (Wistar Inst. Anat. Biol., Philadelphia, Pa.) and V. Defendi. J. Nat. Cancer Inst. 44(1):125-132, 1970.

Polyoma virus, inoc. s.c. into newborn NZW rabbits, resulted in small inj. site nodules within 2 mo., which regressed. One yr. later, 2/12 rabbits developed large fibrosarcomas at the inj. site. These tumors were devoid of the lymphoid infiltration characteristic of primary regressing nodules, the multiple metastases through almost all parenchymal organs. Serum from the 2 rabbits contained polyoma T antibody. Three cell lines which were derived from s.c. or metastatic nodules. Each line contained intranuclear polyoma T antigen (by immunofluorescence) and 1/3 was definitely aneuploid. These cell lines were maintained in tissue culture for over one yr. without the detection of polyoma virus. Attempts at homologous s.c. and intracerebral transplantation of the cultured tumor cells were unsuccessful.

- 70-868 YABA TUMOR VIRUS. II. STUDIES ON INACTIVATION AND REACTIVATION. (E.) Behbehani, A. M. (U. Kansas Sch. Med., Kansas City), S. Barrick and C. R. Bolano. Proc. Soc. Exp. Biol. Med. 132(2):738-742, 1969.

Yaba virus lost all tumorigenic capacity in adult rhesus monkeys after heating at 56°C for 1 hour at pH 3 (pH 5, 7, or 9 had no effect), and after exposure to UV for less than 30 seconds (vaccinia and pox virus were slightly more resistant). UV-inactivated Yaba virus (irradiated 1 min.), mixed with active vaccinia virus and inj. s.c. into 2 monkeys, induced histiocytomas similar to those found in monkeys given active Yaba virus at all sites of inoc. Tumor extracts fixed complement with both anti-Yaba and anti-vaccinia sera. In tumors passed 2 and 3 times in monkeys, complement fixation and hemagglutination-inhibition antibodies to Yaba were readily detected, while those of vaccinia were very low. The tumorigenic capacity of Yaba virus-induced homogenate (first passage) was only partially inhibited by Yaba antisera, while homogenates from later passages were completely neutralized. Vaccinia antisera showed no inhibitory effect.

- 70-869 SUPERINFECTION OF TUMORS WITH VIRUSES. (E.) Sinkovics, J. G. (U. Texas M. D.

Anderson Hosp Tumor Inst., Houston) and C. D. Howe. Experientia 25(7):733-734, 1969.

- 70-870 THE AVIAN LEUKOSIS COMPLEX. (E.) Helmboldt, C. F. (U. Connecticut, Storrs) and T. N. Fredrickson. Nat. Cancer Inst. Monogr. 32:29-42, 1969.

- 70-871 MURINE LEUKEMIA LIKE VIRUS AND THE IMMUNOPATHOLOGICAL DISORDERS OF NEW ZEALAND BLACK MICE. (E.) Mellors, R. C. (Hosp. Special Surg., New York, N. Y.). J. Infect. Dis. 120(4):480-487, 1969.

- 70-872 BIOLOGICAL DIFFERENCES BETWEEN ONCOGENIC AND NON-ONCOGENIC ADENOVIRUSES IN VARIOUS KIDNEY CELLS. (Jap.) Iwameji, Y. (Tokushima U. Sch. Med., Japan). Shikoku Acta Med. 25(2):362-374, 1969.

- 70-873 ONCOGENIC ACTIVITY OF ADENOVIRUS TYPE 12 IN NEWBORN AND EMBRYO HAMSTERS. (Jap.) Aoki, T. (Tokushima U. Sch. Med., Japan). Shikoku Acta Med. 25(2):350-361, 1969.

- 70-874 EFFECT OF TEMPERATURE ON SYNTHESIS OF T AND U ANTIGENS OF PAPOVAVIRUS SV40 AND INDUCTION OF THYMIDINE KINASE. (E.) Vonka, V. (Res. Inst. Immunol., Prague), J. Kára, L. Katinová and H. Zavadová. Arch. Ges. Virusforsch. 28(2):251-254, 1969.

- 70-875 SELECTIVE EFFECTS OF ANTI-MACROPHAGE SERUM, SILICA AND ANTI-LYMPHOCYTE SERUM ON PATHOGENESIS OF HERPES VIRUS INFECTION OF YOUNG ADULT MICE. (E.) Zisman, B. (Nat. Inst. Med. Res., London), M. S. Hirsch and A. C. Allison. J. Immun. 104(5):1155-1159, 1970.

- 70-876 MACROPHAGES AND AGE-DEPENDENT RESISTANCE TO HERPES SIMPLEX VIRUS IN MICE. (E.) Hirsch, M. S. (Massachusetts Gen. Hosp., Boston), B. Zisman and A. C. Allison. J. Immun. 104(5):1160-1165, 1970.

- 70-877 PREPARATION OF INFECTIOUS CELL-FREE HERPES-TYPE VIRUS ASSOCIATED WITH MAREK'S DISEASE. (E.) Cook, M. K. (NIH, Bethesda, Md.) and J. F. Sears. J. Virol. 5(2):258-261, 1970.

See also abstract nos.: 575,576,577,578,579,580,586,594,617,653,730,919,973,978,981

878 ASSOCIATION OF BURKITT'S TUMOUR AND HOLOENDEMIC MALARIA IN WEST NILE DISTRICT, UGANDA: MALARIA AS A POSSIBLE AETIOLOGIC FACTOR. (E.) Kafuko, G. W. (East African Virus Inst., Entebbe, Uganda), N. Baingana, E. M. Nantaght and J. Tibemanya. E. Afr. Med. J. 16(7):414-436, 1969.

Survey of the West Nile region and 13 other districts in Uganda (May, 1967; July and Oct., 1968; Feb., 1969) showed that areas holoendemic for malaria (74-95% occurrence in the 1-yr.-old population) were those positive for Burkitt's tumor (having at least 1 case), and all negative areas were hyperendemic or less (47-75%). There were no cases of Burkitt's tumor (BL) where malaria was hypoendemic or absent. Both diseases were prevalent on the lower open plains in the northern and central parts of the country; the incidence decreased away from these areas. The highest parasite density index was found in children 0-9 yr. of age, with a higher incidence in the 0-4-yr.-old children from BL positive areas (3.96) as compared to that age group in BL negative regions (2.76). There was no difference in the relative prevalence of mosquito or malaria species.

879 CANCER EPIDEMIOLOGY. III. A STUDY BASED ON ISRAELI STATISTICS. (Ger.) Lerner, G. (Bei der Ochsenweide 6, Tübingen, Germany). Med. Welt. 20(19):1103-1110, 1969.

Cancer mortality rates for the years 1958-1961 (inclusive) were expressed as a percentage of rates for 1950-1954 (inclusive) for Israelis of Occidental origin or ancestry, as compared to Israelis of non-Occidental (Near-Eastern and North African) ancestry, as follows: esophagus = 2% and 100%, resp.; stomach = 83% and 103%, resp.; colon = 122% and 325%, resp.; rectum = 68% and 142%, resp.; pancreas = 86% and 160%, resp.; lung = 130% and 160%, resp.; lung (men aged 54 yr., only) = 176% and 216%, resp.; breast (men only) = 114% and 172%, resp.; breast (men over 45 yr., only) = 112% and 149%, resp.; uterus = 54% and 103%, resp.; uterus (women over 45 yr., only) = 68% and 119%, resp.; prostate = 9% and 154%, resp.; lymphatic and hematopoietic systems = 132% and 135%, resp. A comparison of reported percentages for cancers of the stomach (men only; Israeli men = 84%), breast (women only) and lung (both sexes) with comparable tabulations from West Germany, Denmark, Norway, Holland, and New Zealand (1961 rate as a percentage of the rate for 1952) showed that "Occidental" Israeli figures paralleled those of these other countries fairly closely, except for mammary cancer, which tended to remain stationary outside Israel. Among "non-Occidental" Israelis, a comparison of the descendants of old-established settlers and new immigrants (by country of origin)

showed significantly increased rates for cancers of the stomach and esophagus among Yemeni immigrants, for cancers of the lung and prostate among Turkish immigrants, for cancers of the larynx among descendants of Turkish settlers, and for cancers of the breast, and lymphatic and hematopoietic systems among Iraqi immigrants.

70-880 ALTERED IMMUNITY AND CANCER RISK: A REVIEW OF THE PROBLEM AND ANALYSIS OF THE CANCER MORTALITY EXPERIENCE OF LEPROSY PATIENTS. (E.) Oleinick, A. (Kaiser Found. Hosp. Permanente Clin., Portland, Oreg.) J. Nat. Cancer Inst. 43(4):775-781, 1969.

A study of the mortality from cancer in 848 white and Negro pts. admitted to the U.S. Public Health Service Hospital at Carville, Louisiana between 1939 and 1963 with diagnosis of leprosy revealed 21 deaths compared with an expected 19.7 (2 observed cases of leukemia or lymphoma; 1.7 expected). The difference was not statistically significant. The lack of excess mortality due to cancer in leprosy pts. does not support the view that pts. with defects in cellular immune mechanisms are more likely to die of cancer, nor that chronic stimulation of the RES is instrumental in cancer of the lymphoid system.

70-881 AN ANALYSIS OF SOME POSSIBLE EPIDEMIOLOGICAL FACTORS INVOLVED IN CARCINOMA OF THE LARYNX. (E.) Svoboda, V. (Reg. Hosp., Ustecky, Czechoslovakia). Neoplasma (Bratisl.) 15(6):677-684, 1968.

A group of 215 pts. (10 females, 205 males) mostly from Northern Bohemia, a densely populated industrial area, were studied from 1962-67. In 1966, 2.86% of the male population in the study region had carcinoma of the larynx and 33.2% had lung carcinoma. Data for the whole country were 2.55% and 21.2%, resp. Prevalence for carcinoma of the larynx in the study area was 7.5/100,000 compared with 6.9/100,000 for the whole country. Pts. were grouped according to their working environment with respect to exposure to substances carcinogenic to the respiratory tract; 34% worked under safe conditions, the remainder under slightly harmful (22.3%) or very harmful (13%) conditions. In a comparison of 205 men with carcinoma of the larynx, 300 men with lung carcinoma, and 320 male controls, there were more heavy smokers in the patient groups. Controls had 22% nonsmokers, carcinoma of the larynx, 2.93%, and lung cancer, 1%. Half of the females with carcinoma of the larynx were medium to heavy smokers. Since there are similar environmental conditions associated with carcinoma of the larynx and of the lung, it is difficult to explain the insignificant rise in morbidity from the former as compared with the definite rise in morbidity from the latter.

70-882 INCREASED INCIDENCE OF NEOPLASIA IN ASSOCIATION WITH CHRONIC LYMPHOCYTIC LEUKAEMIA. (E.) Hyman, G. A. (Columbia U. Coll. Phys. Surg., New York, N. Y.). Scand. J. Haemat. 6(2):99-104, 1969.

A study of 209 consecutive pts. (82 females, 127 males) with chronic lymphocytic leukemia and/or lymphocytic lymphosarcoma (seen at 2 hospitals in New York City), revealed 72 cases (34.4%) of at least 1 additional neoplasm in a 24-yr. period (1945-68). The control expectation of any single malignancy is 5.4%. Most frequent sites of malignant neoplasms were colon, rectum, skin, breast and lung. Chronic lymphocytic leukemia or lymphocytic lymphosarcoma preceded or was present at the time of diagnosis of the second neoplasm in 49/72 pts. The av. length of time the disease preceded the second neoplasm was 4.6 yr., with a range of 4 mo. to 17 yrs. Av. length of time a malignancy preceded the study diseases was 7.4 yr. with a range of 5 mo. to 32 yr.

70-883 THYROID CANCER IN ISRAEL. (E.) Modan, B. (Tel Hashomer Govt. Hosp., Israel), Z. Eisenstein and I. Virag. Brit. J. Cancer 23(3):488-492, 1969.

In a detailed hospital search in Israel during 1960-65, 343 Jewish pts. had newly diagnosed thyroid cancer. The mean annual incidence was 2.8/100,000 with a female:male ratio of 2.3:1. There were no significant differences in incidence rate based on place of birth (Israel, Asia, Africa, Europe, America), time of immigration and rural or urban residence. Papillary adenocarcinoma made up 50-64% of tumor types below 60 yr. and was reduced to 37% in the older age group. Follicular adenocarcinoma also decreased with age, from 24.3% in the 0-19 yr. group to 14.9% in the older age group. Undifferentiated carcinoma increased from zero below the age of 20 to 4.3% in the 20-39 age group and 26.4% in old age. In view of these data, and the findings of no difference in incidence rate between white and Negro pts. in an American urban study and no difference between Chinese and Malaysian residents in Singapore, it seems likely that an endogenous etiological factor is present.

70-884 REPORT ON 151 CHILDHOOD MALIGNANCIES OBSERVED IN JAMICA. (E.) Bras, G. (U. West Indies, Jamaica), H. Cole, A. Ashmeade-Dyer and D. C. Watler. J. Nat. Cancer Inst. 43(2):417-421, 1969.

During 1958-1967, 151 tumors occurred in children (93 males and 58 females) under 15 in the Parish of Kingston and St. Andrew. These composed 2.9% of all malignancies reported. Among the cancers, one-third were leukemias, the most common form,

and these occurred chiefly in the 0-5-yr. age group. Retinoblastomas were relatively common and exceeded the total number of neuroblastomas and Wilm's tumors. Kaposi's sarcoma was absent and hepatomas rare. The incidence pattern was similar to that seen in the U.S. and Western Europe and varied significantly from Uganda and Western Nigeria. This was unexpected since 65% of the Jamaican population is Negro, 30% a mixture of Negro and European.

70-885 THE CONTRIBUTION OF THE VOLUNTARY AGENCY HOSPITAL TO CANCER EPIDEMIOLOGY. (E.) Burkitt, D. P. (Med. Res. Council, London), E. H. Williams and L. Eshleman. Brit. J. Cancer 23(2):269-274, 1969.

In spite of a lack of diagnostic equipment, and qualitative and quantitative defects in hospital records, it is thought that the data from mission hospitals can contribute to localization of specific disease patterns within a given geographic area. Data from 7 church hospitals situated within a 150-mile radius of each other in East Africa were presented and the ratio of different cancer types compared. Cancer of the stomach was high in Ndolage, Kagondo, and Kaimosi, cancer of the esophagus high in Kagondo, Maseno and Kaimosi, Burkitt's lymphoma high in Kuluva, Shirati and Maseno, Kaposi's sarcoma high in Kuluva, and penile cancer high in Ishaka and Ndolage.

70-886 FAMILIAL OVARIAN CANCER. (E.) Lewis, A. C. W. (Med. Res. Council, Headington, Oxford, England) and B. C. C. Davison. Lancet 2(7614):235-237, 1969.

A description of a family where the mother and 5/7 of her daughters had ovarian cancer. In the next generation, 5/8 females elected to have prophylactic oophorectomy. The ovaries were histologically normal. There was no evidence of testicular tumors in the family members. No other evidence of a hereditary relationship is given.

70-887 THYROID CANCER IN OLMSTED COUNTY 1935-1965. (E.) Verby, J. E. (U. Minnesota, Rochester), L. B. Woolner, F. T. Nobrega, L. T. Kurland and W. M. McConeahey. J. Nat. Cancer Inst. 43(4):813-820, 1969.

Residents of Olmsted County, Minnesota (excluding pts. admitted to the Mayo Clinic from elsewhere) with histologically diagnosed thyroid cancer ranged in age from 11-91 yr., with a mean age of 50 yr. The annual incidence rate/100,000 population (age-adjusted to the U.S. white population for 1950) increased from 1.7 in 1935-44, to 3.1 in 1945-54 to 3.6 in 1955-65. The female:male ratio in 1935-65 was approx. 3:1. If

ult" cases were included in the data, the adjusted incidence rates for the 3 periods 2.2, 3.7, and 6.1/100,000, resp. The increased detection of "occult" tumors is thought responsible for the upward trend in incidence based on data from cancer registries and clinical and autopsy series.

88 CAUSES OF DEATH AMONG ANESTHESIOLOGISTS: A 20-YEAR SURVEY. (E.) Bruce, D. L. Northwestern U. Sch. Med., Chicago, Ill.), Eide, H. W. Linde and J. E. Eckenhoff. *Anesthesiology* 29(3):565-569, 1968.

Between 1947 and 1966 (inclusive), 441 deaths were recorded among junior, active and retired members of the American Society of Anesthesiologists living in the U.S. or Canada. Malignant tumors caused 71/441 deaths (16.1%). Compared to causes of death of U.S. white males and of policy holders with the Metropolitan Life Insurance Company, anesthesiologists seemed to have fewer deaths from neoplasms of the digestive and respiratory systems (23 and 9 cases, resp.; -0.68 and 0.30-0.32 of the expected numbers, resp.), and relatively high death rates from thyroid-RES tumors (17 deaths observed, 8.9 expected). Deaths from leukemia were about equal to the expected numbers.

89 OCCUPATIONAL CANCER OF THE SKIN - A DECLINING DISEASE? (E.) Cameron, L. Edinburgh Health Social Services Dept.). *Edinb. Med. Bull.* (Edinb.) 27(2):17-20, 1969.

Between 1949-1966 (inclusive), the annual death rates from skin cancer (excluding melanoma) in England and Wales fell by 49.7% in males (21.72 to 10.92/10⁵/year) and by 48.8% in females (15.58 to 7.98/10⁵/year). This decline in skin cancer deaths was attributed in part to improved medical care and partially to improved personal hygiene. The thesis that many skin cancers are of occupational origin was supported by the male prevalence during most of this period; the male:female ratio of skin cancer deaths was 1.39:1 in 1949 and 1.36:1 in 1966. In 1962-1965, the annual skin cancer death rate/million in England and Wales increased in females (8.60 to 9.68), while the death rate/million in males decreased slightly in 1961-1964 (12.52 to 9.52). A similar pattern was seen for the annual skin cancer death rates in Scotland for 1959-1961, which increased in females (23.21 to 25.55/10⁵ population) and decreased in males (31.06 to 29.97/10⁵ population). Since the estimated latent period for occupational skin cancer is 10-25 yr., it is suggested that this temporary trend (later reversed in both sets of data) reflected occupational exposure to carcinogenic agents in women during World War II, while the men were in the armed services.

70-890 FIFTY-TWO FORMS OF CHILDHOOD CANCER: UNITED STATES MORTALITY EXPERIENCE, 1960-1966. (E.) Miller, R. W. (NCI, Bethesda, Md.). *J. Pediat.* 75(4):685-689, 1969.

Examination of death certificates for the 29,457 children (under 15) who died of malignant tumors in the entire U.S. in 1960-1966 (inclusive), and for 2487 adolescents (aged 15-19 yr.) dying of cancer in 48 States (excluding Louisiana and Missouri) in 1965-1966, showed annual mortality rates/million in these 2 age groups of 71.47 and 88.76, resp., for all tumors combined. Leukemia was the most frequent tumor in both the children and the adolescents (mortality rates were 34.55 and 26.30/million/yr., resp.). In the children, the next most frequent forms of cancer were brain tumors, lymphomas, neuroblastoma, Wilms' tumor, bone tumors, rhabdomyosarcoma, liver tumors, retinoblastoma and teratoma, in decreasing order. In the adolescents, the next most frequent tumors were lymphomas (all types of lymphoma, especially Hodgkin's disease, were more frequent in this age group than in the children), bone tumors, brain tumors, rhabdomyosarcoma, teratoma, melanoma, embryonal sarcoma, neuroblastoma and liver tumors, in decreasing order. The annual death rates/million for most tumors (excluding neuroblastoma, retinoblastoma and Wilms' tumor) were higher in the 15-19 yr. age group than in the children. Several tumors showed dynamic changes in mortality rates by a single yr. of age.

70-891 DIABETES AND CANCER. (Ger.) Grosse, H. (Path. Inst., Stralsund, Germany). *Geschwulstforsch.* 33(2):149-156, 1969.

Review of different clinical studies showed that the av. frequency of cancer among living diabetics is 2.4% (871/36,135) and according to autopsy study 9.7% (1,010/10,477). It was lower in diabetics with cardiac involvement (9%), encephalomalacia (4.6%), liver cirrhosis (8.1%) or tuberculosis (5.3%) than in diabetics without complications (14.8%). Cancer was found in 29% of the non-diabetic pts. in this autopsy study. The most frequent localization of 153 malignant tumors in 150 diabetics (autopsy) was the stomach (29), liver and gallbladder (18), intestines (16), pancreas (15), lungs (14), breast (11), uterus (11), sarcoma (7), skin (6), prostate (5), leukemia (5), brain (5), kidney (4), ovary (4), larynx (2), esophagus (1). Since the difference in incidence of malignancy between diabetics and non-diabetics decreased with age (from 3% among diabetics and 20.1% among non-diabetics in the 30-39-yr. age group, to 16% and 32.1%, resp., in the 50-59-yr. age group and 16.2% and 20.1% resp., in the 80-89-yr. age group) and the incidence steadily increased (from 1.5% in 1898-1914 to 11.3% in 1956-1957), it is concluded that the lower prevalence of malignant tumors among diabetics is due to their shorter survival caused

by vascular and inflammatory complications. Thus the risk of cancer is not lower in diabetics than non-diabetics.

70-892 MORBID CONDITIONS AT DEATH IN OLD MEN. (E.) Lake, B. (Lidcombe Hosp., Sydney, Australia). *J. Chronic Dis.* 21(11-12):761-779, 1969.

Malignant tumors were found in 20.6% of 713 men aged 70-99 yr., autopsied at the author's hospital over a 4-yr. period. The most frequent malignant tumors were prostate, lung, colon and stomach carcinomas and brain tumors. Benign tumors were seen in 3.8%. Tabulations of statistical associations/dissociations (using 2 x 2 contingency tables) were statistically significant for 172/2630 combinations of diseases. Significant associations of main and contingent conditions were seen between: all malignant tumors and pulmonary abscess; prostate cancer and anatomical urinary tract lesions or upper urinary infections; brain tumors and arterial stenosis, chronic bronchitis and prostatic hypertrophy; lung carcinoma and bronchopneumonia, emphysema, pulmonary tuberculosis and pulmonary abscess; and stomach carcinoma and venous lesions or nephrosclerosis. Significant dissociations were seen between: hiatus hernia and esophagus cancer; hypertrophy and carcinoma of the prostate; and all malignant tumors and cardiac hypertrophy, old or recent cerebral softening and old myocardial lesions. Some of the reverse combinations (with the above tumors as the contingent conditions and the other diseases as the main conditions) were also significant. A significant statistical dissociation of malignant tumors, atheroma and infection from each other was seen. Gross atheroma, major infections, malignant tumors and the median number (6) of lesions found, did not increase with age.

70-893 MALIGNANCIES IN THE ELDERLY. ANALYSIS OF NECROPSY RECORDS FROM HARBORVIEW HOSPITAL, SEATTLE. (E.) Sherwood, K. K. (500 Wall St., Seattle, Wash.). *Northwest Med.* 68(5):448-452, 1969.

From 1946-1966, 2259 malignant tumors were found in 2097/7020 autopsied pts. in the over-65 age group. During the 20-yr. period 1946-1965, autopsies were performed on 58% of all pts. over 65 who died at this hospital (the rate was 47% in 1946-1950 and 67-72% thereafter). The 2259 autopsied pts. over 65 who died with cancer (or histories of malignant diseases) during this 20-yr. period comprised 12% of all deaths, 18.5% of all autopsies, and 32% of all autopsies in pts. over 65. Multiple primary tumors were noted in 162 pts. (7.5%), including 25/50 pts. who survived more than 10 yr. following the diagnosis of the first tumor. Autopsy examination disclosed 391 tumors (17%) which had not been identified clinically. It is concluded that cancer is often

not found until autopsy in the over-65 age group; therefore, that statistics based on death certificates represent only minimal numbers of tumors in this age group.

70-894 TUMOR BIOLOGY - ITS IMPORTANCE IN CLINICAL MEDICINE. (E.) Hrushovetz, S. B. (Winnipeg Clin. Res. Inst., Canada). *Winnipeg Clin. Quart.* 21(3-4):152-173, 1968.

Little change in the annual mortality rate/100,000 population (males and females) from all tumors combined, was seen in Canada between 1962 and 1966. The death rates from cancer of the breast (females) and lung (males) increased by about 10% and 15%, resp., during this period. In women over 25 in Manitoba, annual morbidity and mortality rates/100,000 population remained approx. constant from 1961 through 1966. Throughout this period, breast cancer comprised 20% of all new cancers and about 20% of all cancer deaths, while cervix cancer caused 5% of all cancer deaths. The reported annual detection rate/100,000 population for cervix cancer increased sharply after the introduction of a screening program in 1963; however, the cervix cancer mortality rate/100,000 remained unchanged (10.4 in 1961, 11.3 in 1966). Detection of early tumors by tissue culture, chromosomal analysis, DNA cytophotometry and autoradiography is discussed. The data suggest that in cancer of the breast and (probably) cervix, changes in cellular DNA content precede the morphological changes characteristic of malignant cells.

70-895 ORAL CANCER INCIDENCE AND MORTALITY IN CANADA AND ABROAD. (E.) Anderson, D. L. (U. Toronto, Canada). *J. Canad. Dent. Ass.* 35(4):192-197, 1969.

Incidence and mortality rates/million/yr. (for 1945-1967 and 1945-1963, resp.) for cancer of the mouth and pharynx, tabulated for the 10 provinces of Canada and 21 other nations, showed wide geographical variations during the study periods. In Canada, a male predominance was seen for all tumors except salivary gland cancer; the highest male:female incidence ratio was seen for lip cancer (10-80:1). Provinces showing high male lip cancer incidence rates also showed low rates for tongue cancer (these Provinces were also predominantly rural); conversely, high tongue cancer incidence rates were associated with low rates for lip cancer. Except for a slight increase in cancer of the tongue and mouth floor in males, incidence rates in Canada in both sexes have not greatly changed. Female mortality rates have remained unchanged and male rates have declined in all Provinces except Newfoundland. Male mortality rates have decreased in most Anglo-Saxon nations, Finland, Austria and the Netherlands; they have remained unchanged in the Scandinavian nations, U.S. whites,

zerland and West Germany; and have increased in the U.S. non-whites, South Africa and Latin nations in Western Europe (France, Italy, Belgium and Portugal). Female mortality rates have remained unchanged in most nations, but mortality rates for both sexes have markedly increased in Israel. The possible role of ethnic and perhaps religious characteristics is mentioned with respect to the high male mortality rates and the high male:female mortality ratios in Quebec and in France, though the male mortality rate is increasing in France and decreasing in Quebec.

96 THE TWO "HIT" AND MULTIPLE "HIT" THEORIES OF CARCINOGENESIS. (E.)
 Hey, D. J. B. (Morrison Hosp., Swansea, Wales). Brit. J. Cancer 23(2):313-328, 1969.

Specific stomach cancer mortality rates/mil-population in women (England and Wales, 1958-1966 inclusive; 10 U.S. cities, 1947; and a 10-year date cohort group), when plotted on a double logarithmic graph, fell into a straight line with particularly good fit at ages 35-80 yr. On a semilogarithmic graph, the points fell on a curve showing a decreasing slope with advancing age. A mathematical model derived to express the "multiple-hit" theory of carcinogenesis showed the same curves when plotted in the same ways. A mathematical model derived to express the "single-hit" theory of carcinogenesis, on the other hand, showed a curved line in a double logarithmic graph and a straight line on a semilogarithmic graph. In a discussion of the pathological bases for the 2 theories, it is shown that these theories are not mutually exclusive, but that the stages of tumor initiation and promotion may result from a number of discrete changes in cellular structure and function.

97 IS STOMACH CANCER MORTALITY REALLY INCREASING IN POLAND? (Pol.)
 Lewicki, J. (Inst. Oncol., Gliwice, Poland). Pol. J. Med. Sci. 19(1):47-53, 1969.

Crude mortality rates for stomach cancer in Poland increased between 1959-1966 from 28.7 to 34.3/100,000 for males and from 19.0 to 24.3/100,000 for females. Contrary to other countries (except for Japan) which show a steady decline, age-adjusted death rates for stomach cancer in Poland showed an increase up to 1963 and then declined to decline. Analysis of data according to age groups, sex and residence (rural or urban) showed that the rate among those younger than 65 yr. remained at about the same level between 1959-1964 and then started to decline. This was more evident for urban areas and for males. The death rate for those older than 65 yr. increased up to 1964 (especially in rural areas), then leveled off. Since this was accompanied by an increase from 50%-80% of deaths certified by physicians (in rural areas) and by a decrease of

"old age" as cause of death from 16% to 8%, it is suggested that the apparent increase in the stomach cancer mortality rate in Poland is due to a better reporting of causes of deaths, especially in rural areas and among older people. The results also indicate that the death rate from stomach cancer in Poland is somewhat higher in rural than urban areas.

70-898 CARCINOMA OF THE RIGHT COLON. (E.)
 Nielsen, J. (Municipal Hosp., Copenhagen), I. Balslev and H.-E. Jensen. Acta Chir. Scand. Suppl. 396:106-113, 1969.

Carcinoma of the right colon in 186 pts. at Municipal Hospital in Copenhagen, ages from 26-88 yr. (av. 68.1), represented 31% of their colon cancer pts. from 1950-1964. The age and incidence was slightly higher in women. More than 50% of the tumors were in the cecum, 34% in the ascending colon and 14% in the right flexure.

70-899 CARCINOMA OF THE GALL-BLADDER. A STUDY OF 390 CASES DIAGNOSED IN FINLAND 1953-1967. (E.) Vaitinen, E. (U. Helsinki). Ann. Chir. Gynaec. Fenn. 59(Suppl. 168):1-81, 1970.

The Finnish Cancer Registry records for 1953-1967 (inclusive) disclosed 504 malignant tumors of the gallbladder. The 390 histologically verified primary gallbladder carcinomas comprised 0.25% of all new malignant tumors seen during this period (0.44% in women, 0.06% in men). The av. annual incidence rate/100,000 population was 0.59 (1.01 in women, 0.13 in men). In the over-60 age group, this rate increased from 3.5 in 1953-1962, to 4.9 in 1963-1967; this increase might reflect a higher rate of diagnosis as well as a true increase in incidence. The female:male ratio was about 8:1. The age distribution was equal in males and females. The median age in the 1963-1967 series was about 5 yr. above the median age in the 1953-1962 series. Histories of cholelithiasis were positive in 228/272 evaluable pts. (83.8%): 212/245 women (86%) and 16/27 men (59%). Symptomatic benign biliary disease had been present, before the diagnosis of gallbladder cancer, in only 48.7% of the pts. with known cholelithiasis; the other 51.3% had silent cholelithiasis. The data suggest a relationship between cholelithiasis and gallbladder carcinoma. No substantial relationship was found between gallbladder carcinoma and histories of other diseases, including liver disease. The total series included 1 familial case of gallbladder carcinoma (a woman whose 2 brothers had died of cancer of the biliary tract).

70-900 LIFE EXPECTANCY OF AMERICAN MEN IN RELATION TO THEIR SMOKING HABITS. (E.)

Hammond, E. C. (Amer. Cancer Soc., New York, N. Y.) J. Nat. Cancer Inst. 43(4):951-962, 1969.

Of 447,196 men born between 1868-1927 who were followed for 5 yr. prospectively from mid-1960 to mid-1965, 39,178 men died, yielding unexpectedly low death rates because of underrepresentation in the study group of ill men and of the lowest socioeconomic groups. By adjusting the study data to the 1959-1961 U. S. life tables for white U. S. males, life expectancy tables in relation to number of cigarettes smoked/day were constructed for U.S. men of ages 25-65. For ages 25 and 35, life expectancy was also tabulated according to the age at which cigarette smoking was initiated. In general, life expectancy was greater among nonsmokers than smokers, decreased with increasing numbers of cigarettes smoked/day, and, as calculated only for ages 25 and 35, increased with increasing age at initiation of smoking.

70-901 SMOKING PATTERNS IN AFRICANS AND INDIANS OF NATAL. (E.) Schonland, M. (U. Natal, Durban, South Africa) and E. Bradshaw. Int. J. Cancer 4(5):743-751, 1969.

A survey of inpatients at Durban Hospital, Durban, South Africa in 1964-1966 demonstrated a close association between lung cancer and smoking (cigarettes and/or pipes), duration of smoking, amount smoked/day, and lifetime tobacco consumption in a comparison of 45 African lung cancer pts. and 90 African noncancer pts. To attempt to account for a previously reported higher lung cancer rate among African males than among Indian males in Durban, the smoking habits of 236 African noncancer pts. were compared to those of 130 Indian noncancer pts. Africans began smoking at an earlier age and used home-rolled cigarettes more frequently. Younger Indians (25-54 yr. old) smoked a greater amount/day than did younger Africans, while older Africans (54-yr.-old or older) consumed more tobacco in their lifetimes than did older Indians.

70-902 PROPOSED INITIAL STUDIES OF THE RELATIONSHIP OF COMMUNITY AIR POLLUTION TO HEALTH. (E.) Mancuso, T. F. (U. Pittsburgh Grad. Sch. Pub. Health, Pa.) and J. S. Mordell. Environ. Res. 2(2):102-133, 1969.

Designs for proposed studies of morbidity and mortality in relation to community air pollution, and experimental studies of the effects of air pollutants on microorganisms, tissue cultures and animals, are presented. Several of the epidemiological studies are described as suitable for surveys of lung cancer morbidity and mortality as related to air pollution.

70-903 BRONCHIOLO-ALVEOLAR CELL CARCINOMA OF THE LUNG. (E.) Tala, P. (U. Helsinki

Clin. Thorac. Surg.), K. Saraste and T. J. Maamies Ann. Chir. Gynaec. Fenn. 57(4):488-492, 1968.

Bronchiolo-alveolar carcinoma was histologically confirmed in 13 pts. seen between 1950 and 1967 in the Clinic for Thoracic Surgery of the University Central Hospital in Helsinki. These pts. represented 0.6% of the 1179 pts. treated for pulmonary carcinoma in the clinic during that period, compared to the relative prevalence of 1-5% reported elsewhere.

70-904 BLOOD GROUPS AND LUNG CANCER. (E.) Ashley, D. J. B. (Morriston Hosp., Swansea, Wales). J. Med. Genet. 6(2):183-186, 1969.

In 1257 men with lung cancer, the over-all distributions of the ABO blood groups were approx. equal to the expected values. However, pts. with proximal tumors showed a significant excess of A and a deficit of O, while pts. with distal tumors showed a significant excess of O and a deficit of A. Blood group frequencies were not significantly different between pts. with operable and inoperable tumors. Pts. with undifferentiated tumors showed a significant excess of O and deficit of B; pts. with differentiated glandular tumors showed a significant excess of B. Pts. with squamous cell carcinoma showed an insignificant deficit of B. An insignificantly below-expected frequency of Rh-negativity was seen in the total pt. group and in pts. with differentiated tumors; Rh-negativity was insignificantly above the expected level in pts. with undifferentiated tumors. The observed variations in blood group distribution are discussed in relation to previously reported findings on blood group distributions in smokers and non-smokers (a deficit of B in heavy smokers; excess of B among non-smokers; excess of Rh-negativity among occasional smokers).

70-905 MORTALITIES DUE TO TUMORS OF THE RESPIRATORY TRACT IN THE MUNICIPALITY OF GENOA. (It.) Izzotti, S. (U. Genoa Inst. Hyg., Italy). G. Ig. Med. Prev. 10(2):210-223, 1969.

A study of mean annual mortality rates (1951-1963 inclusive) for malignant tumors of the buccal cavity, pharynx, larynx, trachea, bronchi and lungs, using both standard mortality figures and a "standardized mortality quotient" (derived by dividing expectancy figures by the number of deaths actually reported and multiplying the result by 100), showed that the Genoese mortality rate for tumors of the buccal cavity and pharynx has tended to remain stationary for both males and females at all age levels; the mortality rate for tumors of the larynx has tended to increase for the male population over 55 yr. of age (only) and to decrease for males under 55 (only). (Genoese mortality rates were uniformly somewhat

higher than those for Italy as a whole, for both age groups, although the national rates showed the same tendencies.) A tendency to a linear increase of the overall mortality rate for tumors of the trachea, bronchi and lungs was demonstrable for both males and females, with the greatest increase seen in both sexes over 55 yr. of age and a slight decrease in both sexes, in the under-35 age group. The overall Genoese mortality rate for these tumors was approx. 50% higher than the rate for Italy as a whole, although it was somewhat lower than the national rate for persons 65 or older.

906 CARCINOMA OF THE CERVIX ASSOCIATED WITH PREGNANCY. (E.) Shaffer, W. L. (Crown-McHardy Clin., Metairie, La.) and A. Merrill. Southern Med. J. 62(8):915-921, 1969.

At the University of Oklahoma Medical Center during 1963-1967, carcinoma of the cervix was diagnosed in 44 women out of 7764 pregnancies during pregnancy or the first 4 mo. of the puerperium; 9/44 were originally referred to this hospital with a suspicion or diagnosis of cervical carcinoma. Pregnancy was present in 44/420 pts. with cervical carcinoma. The 44 pts. were generally of low socioeconomic status, were an av. 29-yr.-old, had an av. of 6 pregnancies, and had delivered their first children at an av. age of 17. The pathologic classification of the lesions included carcinoma in situ in 26/44, microinvasive carcinoma in 7/44, and invasive carcinoma in 11/44.

907 CERVICAL CONIZATION IN PREGNANCY. (E.) Bolognese, R. J. (Pennsylvania Hosp., Philadelphia) and S. L. Corson. Surg. Gynec. Obstet. 128(6):1244-1246, 1969.

During 1962-1967 (inclusive), 19,343 infants were delivered at the authors' hospital. All pregnant women underwent prenatal cytological screening. Suspicious or positive cytological smears were found among the 7751 private pts. Among the 592 ward pts., 12 carcinomas in situ (0.10%) and 1 Stage I squamous cell carcinoma (0.1%) were detected by prenatal cervical conization among a total of 33 pts. showing Class 3, 4 or 5 cytological lesions (25/33, 7/33 and 1/33, resp.). Only Stage I tumor was found in a pt. with Class 3 smear. The other 20 pts. undergoing prenatal cervical conization showed varying degrees of dysplasia.

908 EXFOLIATIVE CYTOLOGY IN THE UNIVERSITY OF CAPE TOWN. (E.) Davey, D. A. (U. Cape Town Med. Sch., South Africa). S. Afr. Cancer Bull. 13(1):5-10, 1969.

In 1967, a follow-up study was made of 28,330 women who had undergone cytological screening at

the Groote Schuur Hospital from February 1, 1963-January 31, 1966. Cervical carcinoma (including carcinoma in situ) was found in 1.06% (0.83% of the white women, 1.33% of the non-white women). Peak ages for both intraepithelial and invasive carcinomas in the non-white women were about 5 yr. lower than in the white women. Comparisons of the cytological and biopsy findings in this group disclosed a relatively high false-positive rate and a false-negative rate of about 1%. In 1965-1967 (inclusive), 192 intraepithelial and 173 Stage I and II carcinomas of the cervix were found among 104,239 pts. screened at the Groote Schuur Hospital, including 105 intraepithelial and 30 Stage I and II tumors detected by cytological examination. The av. cytological detection rates/1000 (1.0 for intraepithelial carcinoma, 0.29 for invasive carcinoma, 1.3 for all carcinomas combined) were believed to represent a true exfoliative cytological detection rate for Cape Town at least.

70-909 OCCURRENCE OF CERTAIN MULTIPLE PRIMARY CANCERS IN FEMALES. (E.) Schoenberg, B. S. (NCI, Bethesda, Md.), R. A. Greenberg and H. Eisenberg. J. Nat. Cancer Inst. 43(1):15-32, 1969.

Two groups of women with cancer of the breast (19,394 pts.) and cancer of the genital organs (18,291 pts.) were followed to observe the risk of developing a second primary cancer of the genital organs or digestive system. Pts. were admitted to Connecticut hospitals from 1935 through 1962. Records were obtained from the Conn. Tumor Registry. Survival was recorded as person-years of observation and the expected number of second primary tumors calculated for each site based on person-yr. of observation and the age-, sex-, and site-specific incidence rates. A 50% or greater excess of observed over expected second primary cancer was found in the following: first primary in breast second in large intestine; first primary in genital organs second in large intestine; first primary in uterine corpus or cervix second in rectum; first primary in breast second in corpus uteri; first primary in breast second in ovary.

70-910 EPIDEMIOLOGY OF UTERINE CERVIX CANCER. PART I. PREVALENCE OF UTERINE CERVIX CANCER. (Pol.) Słomska, J. (Inst. Oncol., Gliwice, Poland). Ginek. Pol. 40(2):197-203, 1969.

Age-adjusted incidence/100,000 of cervical cancer in different countries (published in 1966) was compared to that in Poland (1964). It was higher in Columbia (100.6), South Africa (52.0), Jamaica (51.4), Puerto Rico (47.1), Chile (44.9) than in Poland (30.1), and lower in Denmark (28.3), Yugoslavia (26.2), Netherlands (18.9), Sweden (17.2), Finland (16), Norway (15.3), USA-New York (14.6), USA-Connecticut (13.6), England and Wales (12.5) and Israel (5.9). In Poland it constitutes

25% of all neoplasms among women as compared to 40% in South Africa and only 2% in Israel. Between 1960-1965 the registered mortality rate from uterine cancer in Poland increased 50%. The increase was especially pronounced in rural areas but this could be due to better reporting and diagnosis. The greatest incidence in morbidity in Poland is found during the menopausal period (45-55 yr.) decreasing in older age groups. This is in contrast to findings for Israel where the incidence increases with age and for Sweden where the highest incidence is found among 35-45 yr. old women.

70-911 ONCOLOGICAL SCREENING DURING ADMINISTRATION OF ANTIGEST, ANTIGEST B, AND BIOGEST IN THE YEARS 1965-1968. (E.) Gross, K. (Oncol. Inst., Prague), S. Štěrba, H. Marková and H. Wolfová. Neoplasma (Bratisl.) 16(5): 557-563, 1969.

By colposcopic, cytological, and, when necessary, histological examination during 1965-1968, no malignant changes were observed in the uterine cervix of 280 Czechoslovak women receiving oral estrogen-progestagen contraceptives for less than 6 mo. to up to 72 mo.

70-912 THERMOGRAPHY IN BREAST CARCINOMA. (E.) Isard, H. J. (Albert Einstein Med. Ctr., Philadelphia, Pa.), B. J. Ostrum and R. Shilo. Surg. Gynec. Obstet. 128(6):1289-1293, 1969.

Thermography is recommended as a preliminary screening test for the detection of benign or malignant breast diseases. A combination of thermography and mammography, in a group of 266 women with biopsy-proven diagnoses of benign or malignant diseases, proved 90% accurate in pts. with malignant disease, if the results of either or both tests were positive.

70-913 MALIGNANT MESENCHYMAL TUMORS OF THE THYROID. (It.) Veronesi, U. (Nat. Inst. Study Cure Tumor, Milan, Italy), N. Cascinelli and F. Preda. Tumori 55(6):417-422, 1969.

Examination of the records of the National Cancer Institute (Milan) for 1928-1968 (inclusive) disclosed 16 malignant mesenchymal tumors (7 polymorphocellular sarcomas, 3 angiosarcomas, 2 reticulum cell sarcomas, 4 fibrosarcomas) of the thyroid, comprising 3.2% of all malignant thyroid tumors seen during that time. The group included 8 males and 8 females, aged 7-73 yr. at diagnosis (2 boys under 15 with fibrosarcomas, 13 adults); 9 pts. were over 50 yr. old at diagnosis. Five pts. had pre-existing thyroid nodules of several yr. duration, with symptoms of 1 week-2 yr. duration, at diagnosis. Disease progression was usually rapid; the 2 apparent cures (13 and 16 yr. after diagnosis) were seen in pts. with fibrosarcomas of the thyroid.

70-914 SOFT-TISSUE SARCOMAS, BREAST CANCER, AND OTHER NEOPLASMS. A FAMILIAL SYNDROME? (E.) Li, F. P. and J. F. Fraumeni, Jr. (NIH, Bethesda, Md.). Ann. Intern. Med. 71(4): 747-752, 1969.

A survey of 649 children treated for rhabdomyosarcoma in the U.S. between 1960 and 1964 revealed 4 families with a pair of young children (3 sets of sibs, 1 set of second cousins) with soft tissue sarcomas; the expected occurrence was 0.06 sib pairs. Each proband had 1 parent with cancer (breast cancer in 3 of the mothers; acute myelocytic leukemia and disseminated skin cancer in 1 father each). The medical history was charted for 5 generations in 1 family, 3 generations in 1 family, and 4 generations in 2 families. A high frequency of neoplasms was found, especially among the younger members of each family, including 11 soft tissue sarcomas, 7 breast cancers, 4 lung cancers, 2 cancers of the pancreas and 2 other tumors. The occurrence of the other neoplasms was entirely in the probands' paternal line in 2 families, and in the maternal line only in the other 2 families. The pattern of involvement in these 4 families suggested transmission by a pleiotropic autosomal dominant gene, its expressivity being limited by age and sex variations and by other environmental and genetic factors. The occurrence of cancer in 1 parent of each child with rhabdomyosarcoma suggested vertical transmission of a carcinogenic agent between generations of genetically susceptible persons. Direct horizontal transmission of carcinogen(s) was ruled out, since the second child affected by soft tissue sarcoma in each family had been born after the first child had died. No evidence of a genetic disorder associated with a high incidence of neoplasms was observed in these 4 families.

70-915 PLASMA CELL MYELOMA AND RELATED DISEASES IN JAPAN: CLINICAL AND IMMUNOCHEMICAL STUDIES ON M-COMPONENTS. (E.) Takatsuki, K. (Kyoto U. Fac. Med., Japan). Acta Haemat. Jap. 31(5):636-663, 1968.

Multiple myeloma (MM) was found in 0.25-0.41% of all autopsies performed in Japan in 1958-1965 (inclusive); the 1965 autopsy series showed about the same numbers of cases of MM, Hodgkin's disease and lymphosarcoma. The MM death rate in Japan in 1964 (0.28/10⁶ living persons) was much lower than in most Western nations (about 1.0/10⁶ in 1949-1953). Primary macroglobulinemia is also rare in Japan. Sera from 215 Japanese pts., mostly with MM and related diseases, contained no heavy-chain disease proteins, 7SγM-globulins or possible new globulins (such as γE). The M-components of these sera differed from the M-components of sera from a group of New York pts. (white and Negro) in several ways. The sera from the Japanese pts. showed a relatively high incidence of L-type among the antigens of the light polypeptide chains, especially the Bence-Jones proteins (B-JP). The approx. K:L-type

ratios in the γ G-globulins and B-JP were 1:1 and 3:1, resp., in the Japanese, compared to 2:1 and 1:1, resp., in the Americans. The Z-type (γ G3) subclass of the γ G-type M-components was found in sera from 1/135 Japanese, 12/138 white and 1/52 Negro pts. The presence of the Gm(a+f+) phenotype among the myeloma globulins in this series of Japanese pts. is considered a characteristic of Orientals. Gm(a) and Gm(f) never exist on the same molecule in Caucasians, while Negroes do not have the Gm(f) genotype.

916 EXAMPLES OF EPIDERMAL FINDINGS

(DERMATOGLYPHS) IN PATIENTS WITH

LEUKEMIA. (Sp.) Aleksandrowicz, J. (U. Cracow, Poland), T. Debski and Z. Schiffer. Folia Clin. Med. (Barcelona) 19(6):328-334, 1969.

Analysis of dactylograms derived from 250 pts. from the Cracow region) with various kinds of leukemia (155 male, 95 female), as compared to those derived from 600 apparently healthy controls of both sexes, using Dalton's system of classification, confirmed a number of significant differences. Radial loops were significantly more frequent among male pts. (47%, as compared to 30% of all controls); radial whorls, among female pts. (43%, as compared to 29% of all controls). The incidence of radial loops among 33 male pts. with chronic granulocytic (CGL) and 63 with chronic lymphatic (CLL) leukemia were 60% and 52%, resp. The incidence of radial whorls among female pts. with CGL and 25 with CLL was 42% and 52%, resp. The possibility is suggested that genetically determined leukemogenic factors may have been operative prior to the fourth mo. of fetal life.

917 MULTIPLE CASES OF LEUKEMIA ASSOCIATED

WITH ONE HOUSE. (E.) McPhedran, P.

and C. W. Heath, Jr. (1600 Clifton Rd. NE, Atlanta, Ga.). JAMA 209(13):2021-2025, 1969.

The house, built in 1946, was occupied as a double house by a total of 12 families until 1952 (the av. period of residence of these 12 families was 1 yr.). In 1966, a 20-yr.-old man, who had been visited this house in 1950-1952, developed acute myelomonocytic leukemia. After conversion of this house to a single-family home in 1952, a member of each of the 3 families who lived there in 1952-1957, 1957-1963 and 1965-present, developed leukemia in 1958, 1963 and 1967, resp. The first of these 3 pts. (a child with acute lymphocytic leukemia) kept chickens in the house during 1955-1956; the possibility of exposure to avian leukosis is mentioned. The second pt. (a woman with acute leukemia) was the great-aunt of the third (a child with apparent Ph⁻negative chronic granulocytic leukemia, later diagnosed probable acute erythroleukemia). In 1946-1957, a total of 52 persons lived in this house (the average age when moving into the house was 20 yr.), and a total of 865 person-yr. of residence; the

expected number of leukemia deaths in this population at risk was 0.3. The only other neoplasm found among these 52 persons was 1 fibroadenoma of the breast. No unusual radiation was detected in the house or its surroundings, or in the urine of the leukemia pt. currently living there (whose mother had undergone X-ray pelvimetry 9 days before his birth) and his father. The 1956-1966 records for this town disclosed 15 leukemia cases (6 were expected), with no other multiple-case residences. The homes of the other leukemia pts. did not cluster near the index house (which is in the center of the community). The 1956-1966 records for metropolitan Atlanta disclosed 4 pairs of leukemia pts. (adults), all in multiple-family residences. These 8 pts. occupied 8 different dwelling units and were not acquainted with each other.

70-918 GENETIC ASPECTS OF LEUKEMIA. (E.)

Zuelzer, W. W. (Wayne State U. Sch. Med., Detroit, Mich.) and D. E. Cox. Seminars Hemat. 6(3):228-249, 1969.

Data on 102 multiple-case families with acute leukemia (AL), chronic granulocytic leukemia (CGL) and chronic lymphocytic leukemia (CLL), excluding families in which the only affected members were twins or siblings, and data concerning AL in twins, were collected from a survey of the literature (143 references). In 77/102 multiple-case families, which showed 2 or more cases of the same type of leukemia, a marked excess of CLL (39% of the families) and a marked deficit of CGL (8%) were found; this virtually excluded a genetic basis for CGL, since 76/77 families were Caucasian (in which population CGL and CLL are about equally frequent). The small number of familial CLL clusters suggested that the role of genetic factors in this disease is minor. In a separate study of leukemia in twins, the results suggest that concordance for AL, even in identical twins, may be determined more by the age at onset than by genetic identity. The association of AL with several genetically-determined chromosomal and immunity disorders, however, suggests that genetic factors may be involved in leukemogenesis in a small minority of cases. It is concluded that leukemia is a "disease of probability," in which genetic factors constitute only one of a large number of determinants, many of which are of greater importance than genetic factors.

70-919 GENETIC CONTROL BY THE hr-LOCUS OF SUSCEPTIBILITY AND RESISTANCE TO

LEUKEMIA. (E.) Meier, H. (Jackson Lab., Bar Harbor, Me.), D. D. Myers and R. J. Huebner. Proc. Nat. Acad. Sci. USA 63(3):759-766, 1969.

Among HRS/J mice with either hr/+ (wild phenotype) or hr/hr (hairless) genotypes, leukemia arises commonly in the hairless group (72%, as compared to 20%, at 18 mo. of age). The s.c. trocar

transplantation of this tumor is equally practicable in both genotypes. Complement fixation tests for mouse leukemia virus (MLV) were correlated with attempts to isolate MLV, the presence of MLV being equally frequent in both genotypes. Since the 2 groups of HRS/J mice differed genetically only at the hr locus, the homozygous state of the hr locus may be responsible for the increased incidence of leukemia, perhaps through increased susceptibility to MLV virus.

70-920 COMPARISON BETWEEN THE RATES OF PROLIFERATION OF INDUCED MALIGNANCIES AND THEIR NORMAL TISSUES OF ORIGIN. (E.) Bertalanffy, F. D. (U. Manitoba, Winnipeg, Canada). Rec. Results Cancer Res. 17:175-185, 1969.

The 6-hr. mitotic rates of epidermis, mammary parenchyma, and liver parenchyma in rats or mice were compared in normal and malignant states. Benzpyrene-induced tumors of hair follicle walls in mice, 7,12-dimethylbenzanthracene-induced mammary carcinomas in female rats, and dimethylaminoazobenzene-induced malignant hepatomas in rats each generally exhibited higher mitotic rates than did normal tissue at corresponding sites. However, the mitotic rates of hair matrix during the growth phase, the mammary gland during the first half of pregnancy, and regenerating liver after 70-75% hepatectomy, exceeded the mitotic rates of the corresponding malignant tissues.

70-921 MAGNITUDE OF PROLIFERATING FRACTION AND RATE OF PROLIFERATION OF POPULATIONS OF LEUKEMIC CELLS IN MAN. (E.) Clarkson, B. D. (Sloan-Kettering Inst. Cancer Res., New York, N. Y.), J. Fried and M. Ogawa. Rec. Results Cancer Res. 17:136-146, 1969.

Autoradiographic methods for measuring the size of the proliferating fraction and generation time of human leukemic cells are illustrated in the case of an 18-yr.-old girl with acute myelogenous leukemia. The factors affecting these parameters, including pt. selection, drug therapy, type of cells and conc. of cells in the bone marrow, are reviewed. (19 references)

70-922 THE EVOLUTION OF TUMOUR CELL POPULATIONS IN HUMAN BLADDER CANCER. (E.) Cooper, E. H. (U. Leeds, England), P. E. Levi, C. K. Anderson and R. E. Williams. Bri. J. Urol. 41(6):714-717, 1969.

Normal human bladder epithelium showed cellular DNA contents predominantly in the diploid range, with smaller numbers of cells (situated on the surface) in the tetraploid and octoploid range, and very few mitotic figures. Studies of the DNA contents of 60 bladder tumors showed a progressive shift of the modal DNA content to higher

values (with a corresponding increase in chromosome number), as transitional cell carcinomas became more invasive. Tumors showing well-defined DNA modes showed relatively little variation in the chromosome number from cell to cell, but wide variations in the chromosome number were seen among the cells of aneuploid tumors. A small proportion of the highly invasive tumors showed DNA contents close to the normal diploid values. Thymidine-³H labeling indices of DNA synthesis, varied widely among tumors of similar degrees of differentiation and invasiveness. Labeling indices for transitional cell carcinomas were generally low. The well-differentiated tumors resembled normal transitional cell epithelium in their low proliferative activities (few mitotic figures and low thymidine labeling indices). Modal DNA contents of these tumors were diploid or nearly diploid. All tumors showed abnormal karyotypes, with wide variations between tumors and between the cells of an individual tumor.

70-923 THE MOSAIC COMPOSITION OF THE DNA CONTENT OF THE EPIDERMAL CARCINOMAS OF MAN. (E.) Manocha, S. L. (Emory U., Atlanta, Ga.), H. D. Steele and H. F. Stich. Z. Krebsforsch. 72(2):144-154, 1969.

Ploidy was measured by determining the DNA contents of metaphase and interphase nuclei from 8 senile keratoses, 12 carcinomas in situ and 12 invasive squamous cell carcinomas of the skin. The senile keratoses and the control preparations (3 healing skin ulcers) always showed nuclear DNA contents in the diploid range. The carcinomas in situ showed a variable degree of mosaicism (ranging from diploid to hexadecaploid), suggesting the presence of several aneuploid cell types side by side in the same tumor. The invasive squamous cell carcinomas usually showed hyperdiploid or hypertetraploid stemlines. The diagnostic value of this method is discussed.

70-924 ASSESSMENT OF INDUSTRIAL BLADDER CANCER HAZARDS FROM EXPERIMENTAL DATA. (E.) Munn, A. (Imperial Chem. Indust. Ltd., Manchester, England). J. Nat. Cancer Inst. 43(1):227-231, 1969.

An essay on the problem of estimating the environmental hazard to workers handling substances shown to be carcinogenic in experimental animals. In assessing industrial bladder cancer hazards, the ultimate question is whether the manufacture or use of a specific compound presents a carcinogenic hazard to the workmen making it or using it in the conditions of exposure. The significance of carcinogenic activity may thus be modified by those physicochemical properties of a compound influencing the ease with which it is absorbed into the body, and by those circumstances of its industrial use determining the extent to which it contaminates the working environment. (9 references)

70-925 HIGH ANTI-EB VIRAL TITER IN SERA OF PATIENTS WITH NASOPHARYNGEAL CARCINOMA: A SMALL-SCALED SEROEPIDEMIOLOGICAL STUDY. (E.) Ito, Y. (Aichi Cancer Ctr. Res. Inst., Lab. Viral Oncol., Nagoya, Japan), T. Takahashi, A. Kawamura, Jr. and S.-M. Tu. Gann 60(3):335-340, 1969.

In normal adult Chinese and Japanese, anti-P3HR-1 cell titers ranged from 1:10 to 1:3560, with more than 95% lying between 1:40 and 1:640, and a peak between 1:40 and 1:160. Titers against THE-3 cells were slightly higher. The reaction of sera from 22 Chinese and 10 Japanese with nasopharyngeal carcinoma differed, with 90% of the former and 60% of the latter having a reaction against P3HR-1 or THE-3 cells at a dilution of 1:640 or higher. Sera from pts. with cancer in the head and neck apart from the nasopharynx, acute and chronic leukemia, malignant lymphoma and other malignancies had approx. normal titers. Sera from pts. with Burkitt's lymphoma also had higher titers. Pts. with nasopharyngeal carcinoma in Africa and North America have high titers against EB virus.

0-926 ARSENIC AND RESPIRATORY CANCER IN MAN: AN OCCUPATIONAL STUDY. (E.) Lee, A. M. (NCI, Bethesda, Md.) and J. F. Fraumeni, Jr. J. Nat. Cancer Inst. 42(6):1045-1052, 1969.

The mortality data of 8047 white male smelter workers who had been exposed to arsenic trioxide during 1938-63 was compared with a cohort control group of white males from the same states. In the study group 1877 deaths occurred, compared with an expected 1634 deaths. Deaths from tuberculosis, respiratory cancer, heart disease and liver cirrhosis were significantly increased. A short analysis of death from these causes revealed a significant excess of deaths only from respiratory cancer. A gradient in incidence of respiratory cancer was associated with the degree of arsenic exposure. There was an inverse relationship between the latent period for development of respiratory cancer and degree of arsenic exposure, with the mean interval between onset of employment and death being 34, 39 and 41 yr. respectively, in heavy, medium and light exposure groups. Respiratory cancer was also positively related to SO₂ exposure. Radiation is not considered a causal factor in respiratory cancer in smelter workers.

-927 TWO EPIDEMIOLOGICAL INQUIRIES INTO THE INCIDENCE OF BLADDER TUMORS IN INDUSTRIAL WORKERS. (E.) Veys, C. A. (British Rubber & Employers' Ass. Papilloma Comm., Health Res. Unit., Birmingham, England). J. Nat. Cancer Inst. (1):219-226, 1969.

From 1948-67, 33 bladder tumors were registered in 30 current rubber factory or ex-factory workers, with 15/30 known to have been exposed

to carcinogenic rubber antioxidants. The latent period for these men was 17.6 yr. (range 4-29 yr.); the mean age was 54 yr. (range, 44-75 yr.). Analysis of tumor registrants showed that 10% of these working between 1934 and 1943 developed bladder tumors by 1968. Differences between the number of cases of carcinoma observed and that expected was statistically significant. In 1965 a Coroner's Notification Scheme was set up to record all cases of urinary bladder tumors and a detailed occupational history was obtained. Between 1965 and 1968, 49 cases of tumor were reported in the county of study. In 16 cases (33%) there was a history of work exposure to carcinogens.

70-928 ESOPHAGEAL AND LUNG CANCERS IN NATAL AFRICAN MALES IN RELATION TO CERTAIN SOCIO-ECONOMIC FACTORS. AN ANALYSIS OF 484 INTERVIEWS. (E.) Bradshaw, E. (U. Natal Cancer Survey Unit, Durban, South Africa) and M. Schonland. Brit. J. Cancer 23(2):275-284, 1969.

A study of 484 African males interviewed at a large Durban hospital from 1964-1966 included 98 cases of esophageal cancer, 45 cases of lung cancer and 341 cases of non-malignant diseases. The cancer group differed significantly from the control group in 4 variables: (1) They used emetics regularly and purgatives frequently, with most of the medicaments being provided by herbalists and witch doctors. It is uncertain what relation these remedies have with onset of cancer. (2) The drinking of local alcoholic concoctions was higher in cancer groups, and pts. with lung cancer consumed more concoctions than those with esophageal cancer. (3) There were more tobacco smokers in the cancer groups than in the controls. Esophageal cancer pts. tended to smoke pipes, and lung cancer pts. smoked cigarettes. Both cancer groups had an excess of males who have smoked for 30 yr. or more as compared with the controls. Both cancer groups smoked more tobacco than the controls; the esophageal group had the highest lifetime consumption, but 15% of the esophageal group never smoked. (4) More cancer pts. were exposed to 1 or more occupational carcinogens than controls. These included petrol/oil and tar/pitch in lung cancer, and lead, asbestos and possibly soot in esophageal cancer. Specific carcinogens were not determined.

70-929 FURTHER CYTOLOGIC AND HISTOLOGIC STUDIES OF BLADDER LESIONS IN WORKERS EXPOSED TO PARA-AMINODIPHENYL: PROGRESS REPORT. (E.) Koss, L. G. (Mem. Hosp. Cancer Allied Dis., New York, N. Y.), M. R. Melamed and R. E. Kelly. J. Nat. Cancer Inst. 43(1):233-243, 1969.

This is the third report of a follow-up study of 503 men exposed to the bladder carcinogen para-aminodiphenyl (xenylamine). Between 1957 and 1968, 35 cases of bladder carcinoma developed. Cytologic examination of urinary sediments usually revealed a latent period with normal cytology

and absence of clinical abnormalities which lasted from several mo. to 8 yr. This is followed by a time of cytologic abnormalities usually due to nonpapillary carcinoma *in situ* with no abnormal clinical symptoms. The third period is one of invasive carcinoma with cytologic and clinical abnormalities. In a study of 13 men with non-papillary carcinoma *in situ*, 7 developed invasive carcinoma at intervals ranging from 1 to 13 yr., 4 continued to have positive cytology, and 2 have reverted to normal cytology. Cytologic studies are considered to be the best technique for early diagnosis. In 3 cases of carcinoma there was a negative cytology.

70-930 THYROID CARCINOMA IN HIROSHIMA AND NAGASAKI. I. PREVALENCE OF THYROID CARCINOMA AT AUTOPSY. (E.) Sampson, R. J., C. R. Key, C. R. Buncher and S. Iijima (Atomic Bomb Casualty Comm., Hiroshima, Japan). JAMA 209(1):65-70, 1969.

A study was made of thyroid material obtained from 2,327 autopsies performed in Hiroshima between January 1957 and February 1968, and 740 autopsies in Nagasaki between January 1951 and September 1967. The prevalence rate for primary carcinoma of the thyroid was 134/740 (18.1%) for Nagasaki and 402/2327 (17.3%) for Hiroshima as compared with 1-4% in an American autopsy series. Sex-specific rates were 254/1,614 (15.7%) for males and 282/1453 (19.4%) for females. The incidence of thyroid carcinoma among females was significantly higher than among males. Papillary carcinoma composed 525 (98%) of the tumors; 518 of these were occult. The prevalence-mortality ratio was 536 to 5 (107.2). When the autopsies were evaluated for radiation received at time of atomic bomb fall, those exposed to 50 rads or more had a significantly higher prevalence of thyroid carcinoma than those who had received no radiation. The relative risk for the 50 rad or more group was 1.41 times greater than the no-radiation group, with an attributable risk of 6.7%.

70-931 EPIDEMIOLOGIC INVESTIGATION OF MULTIPLE PRIMARY CANCER OF THE UPPER ALIMENTARY AND RESPIRATORY TRACTS. I. A RETROSPECTIVE STUDY. (E.) Wynder, E. L. (Sloan-Kettering Inst. Cancer Res., New York, N. Y.), H. Dodo, D. A. Bloch, R. C. Gantt and O. S. Moore. Cancer 24(4):730-739, 1969.

A retrospective study was made of 104 pts. with multiple primary cancers of the mouth, pharynx and larynx. The women developed their first and second primary tumors at a slightly younger age than men and the interval between diagnosis of the 2 primaries ranged from 8 mo. to 30 yr., 9 mo. in women and 2 mo. to 26 yr., 11 mo. in men. Both tumors arose in the same anatomic region in 26% of the men and 19% of the women. Most commonly, the first primary occurred in the anterior

two-thirds of the tongue or the intrinsic larynx in men, and the anterior two-thirds of the tongue and the floor of the mouth in women. In comparison with a control group of 776 male single primary pts., 97% of the double primary pts. and 87% of the single primary pts. smoked more than 20 cigarettes a day preceding diagnosis. There were no non-smokers in the former group and only 3% non-smokers in the single primary group. In the former group, 53% smoked more than 2 packs a day compared with 43% of single primary pts. The double primary pt. who smoked 2 packs a day before initial diagnosis, developed second primaries within 9 yr. Among the women who developed a second primary within 9 yr., 22% smoked more than 2 packs a day compared with 13% of 249 single primary controls. In a comparison of smoking habits after diagnosis of the first primary, 55% of the men and 63% of women who developed a second primary and 28% of the men and 25% of the women in the single primary group continued to smoke. There was also a significantly higher frequency of radiation therapy in male pts. who developed second primaries 10 or more yr. after the first. Continued alcohol consumption had no significant effect on the occurrence of a second primary tumor.

70-932 FACTORS ASSOCIATED WITH CANCER OF THE ESOPHAGUS, MOUTH, AND PHARYNX IN PUERTO RICO. (E.) Martínez, I. (Cent. Cancer Registry, San Juan, Puerto Rico) J. Nat. Cancer Inst. 42(6):1069-1094, 1969.

A case-controlled, community-based study was made of 400 pts. with epidermoid carcinoma of the esophagus, mouth and pharynx diagnosed in all hospitals and clinics in Puerto Rico during 1966. Each pt. was matched with 3 controls, one from the same hospital or clinic and 2 residents of the same community for at least 10 yr. Among the 400 lesions, 179 were in the esophagus (120 in males, 59 in females) with 52% of them in the middle third of this organ, 153 were in the mouth (115 in males, 38 in females) with 40% and 50% in the tongue of males and females, resp. and 68 were in the pharynx (55 in males, 13 in females), with 45% in the hypopharynx. Overall male-female ratio was 2.6:1. The pts. with epidermoid carcinoma differed significantly from controls in their higher consumption of alcohol, tobacco, hot beverages (mostly coffee) and spices. They also had more irregular eating patterns, had fewer meals per day and a smaller amount of food per meal, which was consumed while very hot and without beverage. The incidence of cancer of the esophagus in Puerto Rico is among the highest in the world; cancer of the mouth and esophagus is also high.

70-933 CANCER MORTALITY AMONG CHEMISTS. (E.) Li, F. P., J. F. Fraumeni, Jr. (NCI, Bethesda, Md.), N. Mantel and R. W. Miller. J. Nat. Cancer Inst. 43(5):1159-1164, 1969.

A study of the mortality data of 3,637 (3,522 males, 115 females) members of the American Chemical Society dying between 1948 and 1967 revealed 444 cancer deaths in males 20-64 yr. old, which compared with an expected value of 354 among all professional men; this was significant. There were 250 cancer deaths in male chemists over 64, which exceeded expectation. Almost half of the excess deaths were caused by malignant lymphoma and carcinoma of the pancreas. Among the 115 deaths of female chemists, 15 were from breast cancer. The large percentage of unmarried women (40%) and high socio-economic status may explain the deviation from an expected number of 7. Suicide accounted for 11% of the deaths, a frequency 5 times that for the U.S. white female population. There was no significant increase in cancer of the skin, lung, or urinary bladder, probably indicating differences in exposures to carcinogenic materials between factory workers and college-educated chemists.

70-934 THIRD CASE OF CHRONIC LYMPHOCYTIC LEUKAEMIA IN A CARRIER OF THE INHERITED Ch¹ CHROMOSOME. (E.) Fitzgerald, P. H. (Christchurch Hosp., New Zealand) and J. W. Hamer. Brit. Med. J. 3(5673):752-754, 1969.

Two males and one female in a seven sibship relationship were carriers of an abnormal G₂ chromosome (Ch¹) and developed chronic lymphocytic leukemia. At time of report, the one other carrier and two noncarrier sibs had normal white blood cell counts, and other carriers in the pedigree were healthy. One sib died at age 50 from carcinoma of the uterus complicated by pernicious anemia. The parents died from sarcoma of the mediastinum and a cerebrovascular accident.

70-935 EPIDEMIOLOGIC AND HISTOLOGIC STUDY OF ORAL CANCER AND LEUKOPLAKIA AMONG 50,915 VILLAGERS IN INDIA. (E.) Mehta, F. S. (Tata Inst. Fund. Res., Bombay, India), J. J. Pindborg, P. C. Gupta and D. K. Daftary. Cancer 24(4):832-849, 1969.

A house to house survey was made of oral cancer and leukoplakia in 4 states in India (Andhra Pradesh, Bihar, Gujarat and Kerala). Within the 50,915 study population, 26 cases of oral cancer were detected (morbidity rates in Europe and the U.S. range from 2.7 to 21.1 per 100,000). In Kerala 12 cases were found and probably were associated with the habit of chewing tobacco and with the presence of submucosal fibrosis. In Andhra Pradesh 10 cases occurred and 9/10 pts. indulged in reverse smoking. The prevalence of leukoplakia in the 4 states ranged from 0.2% to .9%. Of 881 pts., 30 were between 15 and 24 yr., 124 between 25 and 34, and 242 between 35 and 44 yr. The oral location of the lesions varied with the smoking habits of the pt., which in turn varied with the cultural pattern of the different states. Leukoplakia on the labial

mucosa was associated with hookli smoking, while lesions on the palate were associated with reverse smoking.

70-936 STATISTICAL STUDIES IN THE AETIOLOGY OF MALIGNANT NEOPLASMS. (E.) Clemmesen, J. (Finsen Inst., Copenhagen). Acta Path. Microbiol. Scand. Suppl. 209:1-171, 1969.

After a chapter on the methods of data collection and evaluation used by the Danish Cancer Registry, the author discusses the recent marked increase in morbidity and mortality rates from testicular tumors in Denmark, especially in the urban areas (from 1943 through 1962, the morbidity rate doubled in Copenhagen). Epidemiologic data on testicular tumors in Denmark are compared with previously reported data from other nations. The greater part of this paper consists of a series of 21 tables: 4 tables of population data (1958-1962), 16 tables of cancer morbidity and mortality data (mostly for 1958-1962) and 1 table on tobacco consumption (1910-1965) in Denmark.

70-937 OCCUPATIONAL CANCER OF THE RENAL TRACT: RECENT DEVELOPMENTS IN EPIDEMIOLOGY AND LEGISLATION IN GREAT BRITAIN. (E.) Owen, R. (Dept. Employment Productivity, London) J. Nat. Cancer Inst. 43(1):253-254, 1969.

Three recent developments with regard to occupational cancer of the renal tract in Great Britain are described: 1) exfoliative cytological studies of the urine of exposed workers; 2) a prospective study of 41,981 male workers aged 35 yr. or over employed in the rubber and cable-making industries; and 3) issuance of 2 codes regulating employment in the manufacture or use of specified chemicals and prohibiting importation into England of certain of these substances. These included β -naphthylamine, benzidine, 4-aminodiphenyl, 4-nitrodiphenyl and their salts.

70-938 SOME BIOCHEMICAL CHARACTERISTICS OF HUMAN BREAST CANCER AND NONMALIGNANT BREAST LESIONS. (E.) Hilf, R. (U. Rochester Sch. Med., N. Y.), H. Goldenberg, R. A. Orlando and F. L. Archer. Proc. Soc. Exp. Biol. Med. 132(2):613-617, 1969.

Patterns of nucleic acid, lipid and enzyme metabolism were studied in 34 specimens of infiltrating ductal carcinoma, 8 specimens of fibrocystic disease of the breast, and in 10 normal specimens. By comparison with the normal tissues, the carcinomas showed significant elevations in pyruvate kinase activity (by 100-fold), glucose-6-phosphate, isocitrate and malate dehydrogenase activities (by 10-15-fold) and levels of free fatty acids and cholesterol (2-3-fold). The RNA/DNA ratio was unchanged. Triglyceride levels and α -glycerol-phosphate dehydrogenase activity were below normal

levels. With respect to DNA, RNA and lipid levels and enzyme activities, the carcinomas showed the highest activity and the normal tissue the lowest, with intermediate values for fibrocystic disease. The biochemical properties of the human breast carcinomas closely resembled those of mammary carcinomas induced in rats by single doses of 7,12-dimethylbenzanthracene, suggesting that the rat tumor may be a valid experimental model of human breast cancer.

- 70-939 PATHOLOGICAL STUDY OF METASTATIC INVOLVEMENT OF THE STOMACH CANCER. IV. HISTOGENESIS AND DEVELOPMENT. (E.) Yamaqiwa, H. (Mie Pref. U. Sch. Med., Tsu, Japan). Mie Med. J. 18(3):183-194, 1969.

Histogenetic studies of 160 resected early stomach tumors from 142 pts. led to the identification of 2 histogenetic groups: papillary and papillotubular adenocarcinomas (89/160 tumors; Group A) and tubular or tubular-mucocellular adenocarcinomas and mucocellular carcinomas (71/160 tumors; Group B). Group A tumors were usually surrounded by marked or moderate intestinal metaplasia (IM), whereas Group B tumors were usually associated with mild or no IM. Group A tumors were found in any regions of the stomach where IM was present, usually more than 3 cm distant from the pyloric-fundic border (all tumors found in the upper portion of the stomach were of Group A). Group B tumors were usually found within 2 cm of the pyloric-fundic border (suggested as the "minor locus" for ulcer formation or carcinogenesis). Ulceration extending to the subserosa was seen in 17/160 tumors (10.6%); another 17 tumors were malignant polyps. Multicentric tumors were seen in 17/142 pts. (11.8%; 2, 3 and 4 tumors in 12, 3 and 2 pts., resp.). It is suggested that stomach cancer can develop in 3 ways: invasion and destruction of the surrounding tissues; extension to the mucosa only by serial transposition of the superficial epithelium and glandular cells; or extension from multicentric sites of origin.

- 70-940 INACTIVATION OF AN X-IRRADIATED TUMOR BY INDEPENDENT PROCESSES IN VIVO. (E.) Maruyama, Y. (U. Minnesota Coll. Med. Sci., Minneapolis), E. Ackerman and F. M. Khan. Int. J. Cancer 4(6):793-798, 1969.

A mathematical model is postulated for the radiation responses of tumor cells *in vivo*, based on the responses to independent processes: the intrinsic cell radiation response (Process 1) and the host's immunological resistance to the tumor-specific antigens (Process 2). A composite dose-effect relationship is described. Results obtained in the LSA mouse lymphoma were in agreement with this model.

- 70-941 MITOTIC INDEX IN THE REGENERATING LIVER OF TUMOR-BEARING MICE. (E.)

Theologides, A. (U. Minnesota Health Sci. Ctr., Minneapolis) and G. F. Zaki. Cancer Res. 29(11):1913-1915, 1969.

Cellular proliferation patterns in the regenerating liver (6-60 hr. after partial hepatectomy) were studied in male and female C3H (Bittner Z) mice bearing s.c. transplants of a spontaneous C3H mouse mammary carcinoma, and in non-tumor-bearing controls. In controls, the mitotic index increased at 48 hr. after hepatectomy; in tumor-bearing mice, this increase in cellular proliferation was seen at 30-42 hr. Liver regeneration reached max. levels at 48 hr. in both tumor-bearing and control mice; after 48 hr., the rates of regeneration were similar in both groups. A marked decrease in the number of mitoses was seen in the tumors by 18 hr. after hepatectomy, but the mitotic rate increased thereafter, reaching preoperative levels at 48 hr.

- 70-942 MATHEMATICAL ASPECTS OF SYNCHRONIZATION OF MITOTIC RHYTHMS IN TUMOR CELL POPULATION. (Rus.) Filippov, A. I. (Inst. Roent.-Pathol., USSR Min. Health, Leningrad). Med. Radiol. (Moskva) 14(5):47-52, 1969.

A mathematical model is developed by the author.

- 70-943 FAMILIAL ACUTE LEUKEMIA. (Hun.) Sóvári, M. (Heves County Council Hosp., Hungary), M. Laub and E. Nánássy. Orv. Hetil. 110(20):1146-1147, 1969.

- 70-944 REVIEW ON THE PATTERN OF DEATH IN KOREA. (Kor.) Kwon, E. H. (Coll. Med., Seoul Nat. U., Korea). J. Kor. Med. Ass. 11(12):972-980, 1968.

- 70-945 IMMUNOLOGIC FACTORS INVOLVED IN THE GROWTH OF PRIMARY TUMORS IN HUMAN OR ANIMAL HOSTS. (E.) Klein, G. (Karolinska Inst., Stockholm) and H. F. Oettgen. Cancer Res. 29(9):1741-1746, 1968.

- 70-946 MATHEMATICAL INVESTIGATION OF GROWTH RATE OF PULMONARY TUMORS. (Jap.) Kawashima, K. (Gunma U. Sch. Med., Maebashi, Japan), T. Kato, T. Tobe, N. Koike, K. Yatoimi, K. Suzuki and M. Kato. Nippon Acta Radiol. 29(3):335-339, 1969.

- 70-947 ARRHENOBLASTOMA IN FIRST COUSINS. REPORT OF TWO CASES. (E.) Goldstein, D. P. (Stanford U. Sch. Med., Calif.) and E. J. Lamb. Obstet. Gynec. 35(3):444-450, 1970.

- 70-948 FAMILIAL EPINEPHRINE-PRODUCING PHEOCHROMOCYTOMA IN COMBINATION WITH MEDULLARY THYROID CARCINOMA. (Ger.) von Studnitz, W. (U. Lund Cent. Lab. Clin. Chem., Sweden) and O. Ljungberg. Klin. Wschr. 48(3):144-148, 1970.

See also abstract nos.: 557,558,561,568,569,574,576,578,581,582,583,584,585,586,693,825,956,970

0-949 FINE STRUCTURE OF MALIGNANCY-ASSOCIATED CHANGES (MAC) IN PERIPHERAL HUMAN LEUKOCYTES. (E.) Clausen, K. P. (Ohio State Univ., Columbus) and E. von Haam. Acta Cytol. Balt. 13(8):435-442, 1969.

Electron microscopic examination of neutrophils from 4 men (41-48 yr. old) with bronchogenic carcinoma showed nuclear projections of heterochromatin with a thickness of about 400 Å, either free or connecting chromatin masses, and bounded by a double membrane containing a cistern. Blebs of this chromatin were seen projecting from the nucleus and enclosing portions of the cytoplasm. Approx. 3-8 cells with blebs were found in each of 9 neutrophils examined at random. It was proposed that this represents a chromosomal dissociation due to a systemic abnormality of mitosis coinciding with cancer.

0-950 DIFFERENCES IN NUCLEAR RIBONUCLEIC ACID OF HUMAN NEOPLASTIC AND NORMAL TISSUE. (E.) Roche, J. G. (U. California Sch. Med., San Francisco), W. Rosenau and M. L. Goldberg. Proc. Soc. Exp. Biol. Med. 131(2):465-468, 1969.

Nuclear and cytoplasmic RNA was extracted from normal and neoplastic (3 renal cell neoplasms, adenocarcinoma of the colon, and a malignant melanoma) human tissues, and compared electrophoretically on acrylamide gels. The nuclear RNA from the neoplastic tissues revealed 4-6 additional bands in the upper fourth of the gel, compared to the normal tissues, which all had similar patterns. Only minor differences were seen in the cytoplasmic RNAs.

0-951 CHROMOSOME STUDIES IN A CASE OF BENZENE-INDUCED ERYTHROLEUKAEMIA. (E.) Forni, G. (U. Milan L. Devoto Clin., Italy) and L. Moreo. Br. J. Cancer 5(5):459-463, 1969.

Peripheral blood and bone marrow specimens were obtained before therapy from a 37-yr.-old woman with acute erythroleukemia (Di Guglielmo type), which had developed after 7 yr. of occupational exposure to benzene. The pt. also had a 1-yr. history of frequent metrorrhagia, also attributed to benzene. Consistent structural chromosomal abnormalities were seen in all metaphases: a karyotype of 46 chromosomes with a pseudodiploid karyotype (deletion of 2 chromosomes of Group E, missing chromosome marker and a minute centric fragment). It is suggested that benzene may induce chromosomal breakage in a stem cell, which then proliferated into an erythroleukemic clone.

0-952 CHROMOSOME STUDIES ON WORKERS EXPOSED TO ATMOSPHERIC BENZENE. THE POSSIBLE INFLUENCE OF AGE. (E.) Tough, I. M. (Western

Gen. Hosp., Edinburgh), P. G. Smith, W. M. Court Brown and D. G. Harnden. Europ. J. Cancer 6(1):49-55, 1970.

Chromosome aberrations (chromosomes from peripheral blood WBC), particularly rings and dicentric, were more frequent than in the general population in 2 groups of factory workers (20 and 12 men, resp.) who had been exposed to 25-150 ppm benzene in the atmosphere for 1-25 yr. On-site controls of the first group (who had not been exposed to benzene) showed an increase in the percentage of chromosomal aberrations; but controls of the second group did not. Chromosome aberrations in the first group were correlated with age; it is concluded that the increase in chromosomal aberrations was due partly to environmental effects and partly to advancing age. A third group of factory workers exposed to 12 ppm benzene in the atmosphere and their on-site controls did not differ from the general population.

70-953 CONGENITAL LEUKEMIA AND DOWN'S DISEASE. (Rus.) Popnikolov, V. S. (N. I. Pirogov Second Moscow Med. Inst.). Pediatriia 48(1):41-44, 1969.

A review of the literature and presentation of 2 personal cases. (19 references)

70-954 UNUSUAL CHROMOSOMAL PATTERN IN A PATIENT WITH ACUTE MYELOBLASTIC LEUKEMIA WHO ALSO PRESENTED AN XY/XO MOSAIC. (It.) Cardini, G. (Riuniti Hosp., Verbania, Italy), R. Clemente and M. Bersi. Arch. Sci. Med. (Torino) 125(9):433-438, 1968.

In a 72-yr.-old man presenting with acute myeloblastic leukemia, chromosomal analysis of mitotic cells obtained from a culture of bone marrow blood showed 2/120 with a karyotype of 46 chromosomes, 71/120 with 45, 40/120 with 44, 1/120 with 90 and 6/120 which had been spoiled by faulty handling. Both the 44- and 45-chromosome lines showed absence of the Y chromosome and the presence of 2 small acrocentrics (each) in the 21 and 22 positions, although both of the 46-chromosome karyotypes were entirely normal. The hypotetraploid mitosis with 90 chromosomes also showed absence of the Y chromosome and the presence of 8 small acrocentrics. It was concluded that the pt. was probably the bearer of an XY/XO mosaic in which the pathological XO line predominated, and that the sudden onset of acute myeloblastic leukemia had been accompanied by the loss of 1 of the acrocentrics belonging to the G group, thus giving rise to the 44-chromosome line.

70-955 INVESTIGATION OF THE SEXUAL CHROMATIN IN NEOPLASIAS AND ITS POSSIBLE RELATION TO THE PROGNOSIS OF TUMORS. (E.)

Varela-Nunez, R. (U. Santiago, Spain) Cancer Cytol. 8(2):4-22, 1968.

The nuclei of 142 malignant tumors (genital, breast and other sites) in women were studied. No relationship was found between the incidence of sex chromatin and the degree of differentiation of the tumor, the degree of invasion, the stromal reaction, the number of mitosis, 'drumstick' formation in polymorphonuclear neutrophils, or histologic type of the tumor. The incidence of sex chromatin in metastases corresponded to that in the parent tumor, and in the case of 2 tumors in 1 individual, each incidence was independent of the other according to type.

70-956 THE FREQUENCY OF CONSTITUTIONAL CHROMOSOME ABNORMALITIES IN PATIENTS WITH MALIGNANT DISEASE. (E.) Harnden, D. G. (U. Birmingham, England), A. O. Langlands, S. McBeath, M. O'Riordan and M. J. W. Faed. Europ. J. Cancer 5(6):605-614, 1969.

Constitutional chromosomal abnormalities were found in peripheral lymphocyte cultures from 8/1149 pts. (0.69%) with various malignant tumors. This frequency is only slightly higher than the frequency of chromosomal abnormalities in normal populations. The chromosomal abnormalities were identified as familial in 5/8 pts. In these 8 pts., no evidence was found to suggest an association of chromosomal abnormalities with either malignant diseases in general, or with an unusual familial incidence of a specific tumor.

70-957 DETERMINATION OF SEX OF TERATOMAS DERIVED FROM EARLY MOUSE EMBRYOS. (E.) Dunn, G. R. and L. C. Stevens (Jackson Lab., Bar Harbor, Me.). J. Nat. Cancer Inst. 44(1):99-105, 1970.

Sex determination by short chromosome count was done in 8 transplantable testicular teratomas derived from 6-day embryos, grafted intratesticularly into adult mice of histocompatible strains 129/SV-S1JCP and C3H/DiSn or (129/SV-S1JCP X A/HeJ)_{F1}. The data indicated 4 male and 4 female tumors. The presence of both male and female tumors indicate that the neoplastic change occurs in the undifferentiated embryonic cells; and that nothing is inherent in the genetic sex of a population of embryonic cells to either inhibit or enhance the development of teratomas, but normal inductive mechanisms are prevented from operating.

70-958 SARCOMAS AND MULTIPLE POLYPOSIS IN A KINDRED. A GENETIC VARIETY OF HEREDITARY POLYPOSIS? (E.) Fraumeni, J. F., Jr. (NIH, Bethesda, Md.), C. L. Vogel and J. M. Easton. Arch. Intern. Med. (Chicago) 121(1):57-61, 1968.

The proband was a 16-yr.-old Negro male with reticulum cell sarcoma and colonic polyps. His sister had died of a retrogastric liposarcoma when she was 17, and a brother had died of a metastatic carcinoma of the colon with multiple polyposis when he was 11. Another sibling died in infancy of ileocolitis; 3 other siblings and the mother were normal. The father of the proband had an unremarkable history until he was 50, when he died of an osteogenic sarcoma metastatic to the lung. No lesions were found in his intestinal tract. The maternal and paternal families showed no evidence of mesenchymal tumors or colonic polyps, but the maternal grandmother had died of carcinoma of the stomach at 72. It is suggested that this syndrome may be a variant of Gardner's syndrome (multiple polyposis with benign mesenchymal tumors). The disease pattern in this family suggests autosomal dominant inheritance of a single mutant, highly penetrant, pleiotrophic gene.

70-959 FAMILIAL CHRONIC LYMPHOCYTIC LEUKEMIA. (E.) Fraumeni, J. F., Jr. (NIH, Bethesda, Md.), C. L. Vogel and V. T. DeVita. Ann. Intern. Med. 71(2):279-284, 1969.

Three cases of chronic lymphocytic leukemia were found among 13 sibs of a family whose parents were second cousins. The sibs lived apart and did not have a common occupation; they were not overly susceptible to infection and skin tests revealed no evidence of anergy, but 3/3 had osteoarthritis, as did 1 non-leukemic sister. An immunoglobulin deficiency and an impairment of *in vitro* transformation of lymphocytes by 0.1 ml of phytohemagglutinin was seen in the 2 surviving sibs with leukemia and in 1 other sib without leukemia; 2 other non-leukemic sibs had a selective immunoglobulin deficiency alone. One other sib had died with carcinoma of the prostate, and 2 additional relatives (a paternal uncle and a maternal aunt) had died with bladder carcinoma. Examination of 22 living members of the third generation of this family showed no abnormal LE preparations or Coombs' tests (direct or indirect).

70-960 MULTICENTRIC FOCI OF CARCINOMAS ARISING IN STRUCTURES OF CLOACAL ORIGIN. (E.) Stern, B. D. (Cedars-Sinai Med. Ctr., Los Angeles, Calif.) and L. Kaplan. Amer. J. Obstet. Gynec. 104(2):255-266, 1969.

Ten women with simultaneously (3) or sequentially (7) developing carcinomas of the vagina, cervix, anal canal and perianal region are described. "Cloacogenic" squamous cell carcinomas of the anal canal and the cervix or vagina were found simultaneously in 2 pts.; 4 other pts. developed carcinomas of the anal canal following treatment for cervix carcinoma. It is suggested that the frequent appearance of multicentric tumors in the

ectocervix, vagina, vulva, anal canal and perianal skin may be explained by their common embryonic origin (cloaca).

- 70-961 CANCERS DEVELOPING AT THE SITE OF AN IDIOPATHIC MEGAESOPHAGUS. (Fr.) Ebray, C. (Clin. Hydrol. Climatol., Paris), Leymarios, J.-P. Étienne and J.-P. Cuq. Arch. Franc. Mal. Appar. Dig. 57(1):5-24, 1968.

Cancers developing at the site of the primary disorder were found in 6/62 pts. with megaesophagus. All of the pts. were men, with a mean age of 53 yr. (range 41-67 yr.) and a mean duration of known megaesophagus of 13 yr. (range 2-32 yr.; 1/8, 20 yr. or more). Among those diagnosed histologically, 2/4 were epidermoid carcinomas; 1/4 was a glandular vegetating papillary carcinoma; 1/4 was a malpighian spinocellular carcinoma. Estimates of the frequency of incidence of this complication, as reported in the literature, ranged from 2-6%. Among a total of 69 cases reported (including these 8), the mean interval between the initial diagnosis of megaesophagus and the appearance of cancer was 20 yr.; the male:female ratio was 78%:22%.

- 70-962 THE PROBLEM OF CARCINOMA IN THE PEUTZ-JEGHERS SYNDROME. (E.) Olansky, S. Memory U. Sch. Med., Atlanta, Ga.) and J. L. Ford. Southern Med. J. 62(7):827-829, 1969.

Carcinoma of the stomach metastasizing to the liver, lymph nodes and diaphragmatic peritoneum, found in a 13-year-old girl with Peutz-Jeghers syndrome, was attributed to malignant degeneration of a polyp(s).

- 70-963 VILLOUS ADENOMAS OF THE COLON, BENIGN OR MALIGNANT? (E.) Olson, R. O., Jr. and W. C. Davis (4101 Woolworth Ave., Omaha, Neb.). Arch. Surg. (Chicago) 98(4):487-492, 1969.

Results of follow-up studies (lasting an av. of 4 mo.) in 97 pts. with 110 villous adenomas of the colon are presented. These tumors were all clinically benign; 39/110 (35.4%) were histologically malignant (invading the muscularis mucosa) and 71/110 (64.6%) were histologically benign; 36.4% of these tumors were above the plicata reflection, and 16/40 tumors of this location were histologically malignant. Adenomatous polyps of the large intestine were seen at diagnosis in 13/97 pts. and 41/97 (42%) showed malignant tumors of other types, including 22 carcinomas of the colon. During the follow-up period, 16/97 pts. (16.6%) developed new tumors of the colon (villous adenomas in 6/16, adenomatous polyps in 8/16, adenocarcinoma or villous adenocarcinoma in 1/16 each). Since the word "adenoma" is commonly used to indicate a benign neoplasm, it is suggested that these neoplasms be called "villous tumors" of the colon.

- 70-964 HISTOPATHOLOGIC AND HISTOCHEMICAL STUDY OF INTESTINAL POLYPOSIS IN RELATION TO THE DEVELOPMENT OF CANCER. (It.) D'Alonzo, U. (San Gerardo Hosp., Monza, Italy). Chir. Pat. Sper. 16(5):468-480, 1968.

Pathologic and histochemical studies of surgical specimens of polyps of the large intestine (32/45 derived from male pts.) showed that 26/45 were adenomatous in type, 15/45 were villous, and 4/45 were juvenile (all 4 from subjects aged less than 20 yr.). Areas of incipient malignant transformation of the mucosa (only) were found in 9/45 (6/9, adenomatous; 3/9, villous; 2/9, with multiple foci of malignization). Phosphomonoesterase activity was higher in polyps undergoing transformation than it was in benign specimens. As compared to the mucosa of benign polyps, alkaline phosphatase activity in malignant polyps was somewhat higher in intact mucosa near, but not bordering on, areas of malignization. (It was also relatively higher at the levels of the epithelium and the stroma, in these areas.) It was considerably weaker in apparently intact mucosa immediately bordering on areas of cancerization, and barely or not demonstrable in actual tumor tissue. These differences suggest the presence of a process of specific metabolic change, preceding malignant transformation.

- 70-965 MULTIPLE SARCOMAS IN MAFFUCCI'S SYNDROME. (E.) Banna, M. (Newcastle Gen. Hosp., Newcastle upon Tyne, England) and G. S. Parwani. Brit. Radiol. 42(496):304-307, 1969.

Maffucci's syndrome (dyschondroplasia with hemangiomas) was diagnosed in a 68-yr.-old man who had noted a swelling of 1 wrist at the age of 12 yr. X-ray examination at the time of diagnosis disclosed several skeletal chondromas and multiple soft tissue phleboliths. The wrist mass was identified as a benign chondroma on 2 occasions over a 5-yr. period. The pt. later showed malignant transformation of 2 other chondromas (of the ankle and knee joint) to chondrosarcomas, and died with a lung metastasis 8 yr. after the diagnosis of Maffucci's syndrome.

- 70-966 METASTASES TO THE PITUITARY GLAND. (E.) Hägerstrand, I. (Gen. Hosp., Malmö, Sweden) and J. Schönebeck. Acta Path. Microbiol. Scand. 75(1):64-70, 1969.

In an autopsy series of 763 pts. with a variety of tumors, pituitary metastases were seen in 29 pts. (3.8%), all of whom had widespread metastases (5 or more organs). The pts. with breast cancer showed a significantly higher frequency of pituitary metastases (12/94 = 12.8%) than the remainder of the group (17/669). The pts. with breast cancer had more advanced disease at autopsy, as shown by the higher frequencies of multiple organ and bone metastases (52% and 49%, resp.) than in the remainder of the group (31% and 22%,

resp.). However, pituitary metastases were significantly more frequent in pts. with breast cancer and metastases to multiple sites and the skeleton (12/50 and 11/46, resp.) than in pts. with other tumors associated with metastases of the same type (17/208 and 12/149, resp.). In the 94 pts. with breast cancer from this group, combined with an additional group of 214 pts., the total frequency of pituitary metastases was 14.9% (46/308 pts.).

70-967 SOME OPINIONS ON CAUSAL RELATIONSHIP BETWEEN CHORIOEPITHELIOMA AND ENDOCRINE MILIEU. (E.) Akasu, F. (U. Kanazawa Sch. Med., Japan), S. Kuwabara, T. Iwakami and J. Sumitani. Endocr. Jap. 16(1):205-210, 1969.

Relationships between host immunity and a postulated feedback interaction between placental steroid hormones and human chorionic gonadotropin (HCG), in normal pregnancy and trophoblastic tumors, were studied. Sera from normal pregnant women (especially women in the first trimester) contained a factor which inhibited the ovarian and uterine response to exogenous HCG in mice. The decrease in HCG titers, seen during the first trimester of normal pregnancy, appears to reflect the influence of a control mechanism on the production of autoimmune antibodies by the host, and that subnormal RES activity, with the resulting low antibody production, might promote the development of the chorionic villi and result in prolonged HCG hypersecretion. Women with chorion-epithelioma and cervix cancer showed subnormal RES function (Congo red indexes). A similar relationship between the placenta and host immunity was demonstrated by 2 experiments in rats. Urinary estrogens (especially estradiol) were very low in pts. with chorionepithelioma. It is suggested that RES hypofunction, resulting from an abnormal decrease in estrogen metabolism during pregnancy, might promote or induce pathological growth of the chorionic villi.

70-968 ONCOGENIC DIFFERENTIATION OF THE INTRA-EPIDERMAL ECCRINE SWEAT DUCT: ECCRINE POROMA, POROEPITHELIOMA AND POROCARCINOMA. (E.) Mishima, Y. (Wayne State U. Sch. Med., Detroit, Mich.) and S. Morioka. Dermatologica (Basel) 138(4):238-250, 1969.

Histological evidence suggesting the range of benign to malignant tumor development, from the poroma (poroacanthoma) to the poroepithelioma to the porocarcinoma, of the eccrine sweat duct, is discussed.

70-969 FACTORS INFLUENCING CANINE MAMMARY CANCER DEVELOPMENT AND POSTSURGICAL SURVIVAL. (E.) Schneider, R. (Viral Rickettsial Dis. Lab., Berkeley, Calif.), C. R. Dorn and D. O. N. Taylor. J. Nat. Cancer Inst. 43(6):1249-1261, 1969.

In a study of 87 bitches with mammary cancers (71 adenocarcinomas; 22 mixed tumors) and 87 age- and breed-matched controls, neutered bitches had 12% of the mammary cancer risk as compared to controls. Bitches spayed before any estrous cycles had 0.5% of the risk; those with only 1 estrous cycle, 8%, and animals with 2 or more estrous cycles before neutering, 26%. In the group with 2 or more estrous cycles before neutering, animals spayed before 2.5 yr. old had a marked decrease in mammary cancer risk not shown in bitches neutered after 2.5 yr. old. Pseudo-pregnancy, parity and fecundity had no significant effects of mammary cancer risk. The younger an animal at the time of cancer surgery, the better its survival chances. Highest mortality was seen in the first yr. after surgery. Neutering after cancer diagnosis did not affect survival or cause of death. Age distribution of breast cancer in the bitch mimics that of women. The authors suggest the use of canine mammary cancer as a research model for cancer in women.

70-970 POSITIVE α_1 -FOETOPROTEIN TESTS IN PYRIDOXINE DEPRIVED BABOONS: RELEVANCE TO LIVER CARCINOMA IN AFRICANS. (E.) Foy, H. (Wellcome Trust Res. Labs., Nairobi, Kenya), A. Kondi, C. A. Linsell, A. M. Parker and P. Sizaret. Nature (London) 225(5236):952-953, 1970.

Baboons were fed a pyridoxine (P)-deficient diet for 118 days to 3 yr.; 5/10 animals had positive serum α -fetoprotein (AFP) tests (highly specific for liver carcinomas in primates and man). Histological changes seen in the livers of 2/10 P-deficient animals at autopsy, were consistent with previously reported changes. AFP-negative results were found in animals on a natural diet, pair-fed controls or animals on a riboflavin-deficient diet. The authors discuss the marginal existence of P in the diet of Africans and suggest its relevance to the high incidence of primary carcinoma of the liver among Africans.

70-971 HISTOCHEMICAL ACTIVITY OF ALKALINE AND ACID NUCLEASES IN RELATION TO THE INCIDENCE OF CARCINOMAS IN THE DIGESTIVE TRACT OF THE RAT. (Fr.) Fort, L. (U. Louvain, Belgium) and H. S. Taper. Path. Europ. 4(1):42-57, 1969.

Acid and alkaline DNase and RNase activities were compared in sections of digestive tract derived from 30 normal Wistar rats of both sexes. Alkaline DNase and RNase activities were greatest in the absorbent areas of the duodenum and small intestine, the crypts of Lieberkühn, the biliary canaliculi, and the excretory tubules of the pancreas. As compared to alkaline DNase activity, the intracytoplasmic activity of alkaline RNase was considerably greater, especially in the endothelial cells of the capillaries. Acid DNase and RNase activities were found primarily in the nuclei, nucleoli and cytoplasmic granules, and were most intense in the villi of the duodenum

and small intestine and the crypts of Lieberkühn. A review of 13 reports in the literature concerning the localization of spontaneous and nitrosamine-induced g.i. carcinomas in the rat suggests that the incidence was greatest in those areas in which DNase and RNase activities were lowest (the esophagus, forestomach, stomach and large intestine); that it was least in those areas in which these nuclease activities were highest, as indicated above. It was concluded that the nucleases may provide both an extracellular (alkaline nucleases) and intracellular acid nucleases) barrier, protecting the integrity of genetic material by excluding exogenous nucleic acids which could induce malignant transformation.

0-972 COMPLEMENT ACTIVITY OF SERA FROM NZB/BL AND NZB/BL x NZW F 1 MICE. (Fr.)
 etourneux, M. (Sci. Res. Inst. Cancer, Villejuif, France), A. Horsch and J.-C. Salomon. C. R. Acad. Sci. [D] (Paris) 270(19):2391-2393, 1970.

method is described for determining mouse serum complement activity. A reference hemolytic system, using a mixture of sheep RBC and rat anti-sheep RBC serum (prepared by immunizing Fischer rats), and using fresh guinea pig serum (diluted 1/8, 1/16, etc.) as a source of complement, permitted determination of 50% hemolytic values, with a curve traced for each serum, expressing hemolysis as a function of dilution. The method is said to be both highly sensitive and reliable, with hemolysis read on a spectrophotometer at 412 mμ or both supernatants and precipitates, thus avoiding distortion of results. In an illustrative study, control sera were derived from 2-4 mo.-old CBA and C3HJ mice. Mean values for both male and female NZB/BL x NZW F 1 mice (20 mature; 7 immature) were consonant with those for controls, but mean values for both male and female NZB/BL mice were significantly below those obtained for the other 3 strains, presumably because of the absence of the third component of serum complement (C₃) in this one line, alone. In the other strains, values for females were consistently lower than those for males (statistically significantly in CBA mice). They were statistically significantly lower for 2-mo.-old female, as compared to male, NZB/BL mice, but somewhat higher for 12-14-mo.-old NZB/BL females, as compared to males. The latter difference was not statistically significant.

0-973 SPONTANEOUS RETICULAR NEOPLASMS IN (CBA X DBA/2)F₁ MICE, WITH SPECIAL EMPHASIS ON THE OCCURRENCE OF PLASMA CELL NEOPLASMS. (E.) Rask-Nielsen, R. (U. Copenhagen) and P. Ebbesen. J. Nat. Cancer Inst. 43(3): 551-564, 1969.

There were 96/213 (43% in males; 57% in females) spontaneous reticular neoplasms occurring in

(CBA x DBA/2)F₁ mice, generally older than 18 mo. The mean survival time for those with reticular tumors was 25.8 mo.; for those without tumors of any kind, 27.2 mo. Types of neoplasms (4 were unclassified): (1) Plasma cell (50) - 35 were typed as grade III; 15 as grade IV. Immunoglobulin gamma G paraproteinemia was found in 16 mice with grade III neoplasms and in only 2 mice with grade IV tumors; gamma A and gamma M were found in 2 mice each with grade III tumors. No Bence Jones protein was observed. Transplantation of the neoplastic cells resulted in a generalized spreading of the neoplasm in 50-100% of the recipients. Production of paraprotein was continued in 10/14 tumors for 5-34 passages. (2) Reticulosarcoma (11) - 6 showed generalized spreading, 3 were limited to the ovaries, 1 to the liver, and 1 to the thymus. (3) Lymphocytic (25) and stem cell leukemia (6). Possible roles of a latent leukemia virus and age-dependent decreases in host immunity in mice of this strain are discussed.

70-974 FIBRINOGEN METABOLISM IN EXPERIMENTAL TUMOURS. (E.) Peterson, H.-I. (U. Göteborg, Sweden), K. L. Appelgren and B. H. O. Rosengren. Europ. J. Cancer 5(6):535-542, 1969.

After i.v. inj. of ¹²⁵I-labeled mouse fibrinogen (0.2 ml), increased uptake was found in tumor tissue as compared with normal muscle and liver; and the uptake was more markedly increased in female C₃H mice bearing mouse mammary tumors than in males bearing 20-methylcholanthrene-induced sarcoma (both tumor types were from established tumor lines transplanted i.m. in a hindleg). When rat fibrinogen (0.3 ml) was used in syngeneic C₃H mice, an increase in fibrinogen uptake in tumor tissue was also seen; the increase was more marked in the sarcomas. This difference was attributed to variance in experimental technique. Antifibrinolysis delayed the disappearance of labeled fibrinogen in the mammary carcinoma, but did not affect the sarcoma. Induced fibrinolysis enhanced the disappearance of the label in both groups.

70-975 THE EFFECT OF A GROWTH-ENHANCING SUBSTANCE, FROM LEUKEMIC CELLS AND NORMAL MOUSE EMBRYO FIBROBLASTS, ON LEUKEMIC CELLS IN TISSUE CULTURE. (E.) Pluznik, D. H. (Govt. Hosp., Tel-Hashomer, Israel). Israel J. Med. Sci. 5(3):306-312, 1969.

A feeder layer of myelocytic leukemic cells (10¹-10⁷ cells/plate), strain P-1081 (radiation-induced), irradiated (1500 R) to inhibit multiplication, was covered with hard agar, on top of which 10³ unirradiated leukemic cells were seeded in soft agar. The plates with 10⁶ irradiated cells had the highest number of leukemic cell colonies and largest colony size. Unirradiated and irradiated (4000 R) mouse embryo fibroblasts, strain HA/ICR, were similarly found to enhance

the growth of leukemic cells, and were essential to growth and maturation of normal granulocytes and macrophages. A dialysis membrane placed over the feeder layer caused a small decrease in the number of leukemic cell colonies, but completely prevented growth of the bone marrow cells. The mouse embryo fibroblasts enhanced the growth of leukemic cells, even when separated by 10 mm of agar, while the effectiveness of the irradiated leukemic cells was diminished.

- 70-976 EFFECT OF TEMPERATURE ON POTASSIUM-DEPENDENT STIMULATION OF TRANSCELLULAR MIGRATION IN NORMAL AND NEOPLASTIC CELLS. (E.) Strom, R. (U. Rome Inst. Biol. Chem.), P. Caiafa, B. Modoví and A. Rossi Fanelli. FEBS Letters 3(5):343-347, 1969.

Patterns of potassium ion (K^+)-stimulated, temperature-dependent transcellular migration of glutamate through a complex membrane, suggested the effects of simple diffusion superimposed on the effects of facilitated and active transport. The cells studied (normal or regenerating liver and Novikoff hepatoma cells from Sprague-Dawley rats) seemed to have individual limiting rates of transcellular glutamate migration, which were reached either by increasing the temperature or by addition of K^+ to 1 side of the membrane. In the absence of K^+ , temperatures required for the max. glutamate migration rate were 38-40° C for the tumor cells, 40-42° C for regenerating liver cells and over 42° C for normal cells. Some heat lability (possibly a property of rapidly proliferating cells in general) was seen with the regenerating liver cells, while the hepatoma cells showed a peculiar heat sensitivity.

- 70-977 CYTOLOGIC MANIFESTATIONS OF NEOPLASTIC TRANSFORMATION IN VITRO. (E.) Barker, B. E. (Rhode Island Hosp., Providence) and K. K. Sanford, J. Nat. Cancer Inst. 44(1):39-63, 1970

Neoplastic conversion occurred in 11/12 embryonic cell lines from C3HF/HeN mice, Syrian hamsters and ALB/N rats. An increase in cytoplasmic basophilia was seen in all cell lines that were neoplastic (producing sarcoma in syngeneic animals in vivo by intraocular or i.m. implant); and most showed 4 or 5 of the progressive cytologic changes observed: increase in number and size of nucleoli; increase in nuclear:cytoplasmic ratio; retraction of cytoplasm; and formation of clusters and cords of cells. Cytological diagnosis of neoplastic transformation (by identifying the above changes) agreed with in vivo assays in 53/54 (98%) examinations of the 5 mouse cell lines; 17/17 (100%) of the 3 hamster cell lines and 18/24 (75%) of the 4 rat cell lines. All cell lines were free of murine leukemia virus complement-fixing antigens, and several were free of Type C particles.

- 70-978 IN VITRO CULTURE OF A CELL LINE DERIVED FROM A HUMAN LYMPHOSARCOMA. 1. CYTO-CHEMISTRY, CYTOGENETICS AND CELLULAR ULTRASTRUCTURE. (Fr.) Suárez, H. G. (Nat. Acad. Med. Inst. Hematol. Res., Buenos Aires), S. Brioux de Salum, S. Pavlovsky, B. Ruibal and A. Pavlovsky. Int. J. Cancer 4(6):880-890, 1969.

After 2 weeks of undisturbed culture in vitro, typical lymphocytes and lymphoblasts derived from a human lymphosarcoma had developed into lymphoid cells suspended in the medium and fibroblasts adhering to the bottom of the flasks. By the end of the fourth week, the cells in suspension had become blast cells which were beginning to multiply steadily; while large round cells had appeared among the fibroblasts, which were beginning to thin out and which disappeared entirely, 90 days after the culture was begun, which continued to grow. The suspended cells were highly irregular and frequently bizarre in form, with no resemblance to the original cells. They were strongly PAS-positive; peroxidase- and both alkaline and acid phosphatase-negative. They were polyploid, with 3-5 times the normal number of chromosomes. Supernumerary chromosomes belonged to the Denver group. Extra chromosomes were found in almost all groups. Chromosomal anomalies were most frequent in tetraploid or near-tetraploid cells, including minute chromosomes in the 21-22 group and 1 or more large, acrocentric, marker chromosomes in 90% of the mitoses. Electron microscopic examination showed 1 or more nuclei, with highly dispersed chromatin and 1 or more large nucleoli/nucleus. The cytoplasm was rich in organelles, with abundant ergastoplasm, ribosomes, and irregularly shaped mitochondria, containing granules similar to those seen in the mitochondria of adenovirus-12-induced tumors. Inclusions were found in 35% of the cells, including inclusions with double membranes among those which could not be interpreted. No cytopathogenic agent was found. The cells contained no complement-fixing antigens related to adenoviruses, polyoma virus or SV40. The transformation suggested either an in vitro mutation (or high degree of selection) in 1 of the 2 types of cell originally present, or the intracellular inclusion of a virus whose characteristics are completely unknown, to date.

- 70-979 FACTORS ASSOCIATED WITH SPONTANEOUS TRANSFORMATION OF HAMSTER CELLS IN CULTURE. (E.) Yaniv, A. (U. Tel Aviv, Israel) and T. Gotlieb-Stematsky. J. Nat. Cancer Inst. 44(2):283-296, 1970.

Spontaneous transformation was more frequent in dispersed-cell cultures of embryonic hamster cells, than in cultures developing after seeding large numbers of cells. Primary cultures from embryos of different ages showed about the same rates of transformation. The only embryonic tissue showing a higher transformation frequency

than any other tissue was lung. The growth of fibroblast-type cells in parallel orientation was promoted by horse serum and inhibited by calf serum. The only cultures which yielded transformed colonies during serial passages were those cultures which contained transformed cells during the primary culturing. The presence of cells containing abnormal chromosomes, even in the primary cultures (especially lung cultures) may account for the transformed cells. After culturing in vitro, transformed clones showed a rapid change from diploid to heteroploid chromosome numbers. Cloned primary cultures yielded cell lines with greater tumorigenicity in hamsters than cell lines obtained from uncloned cultures. The generation times and growth potentials of the cloned cell lines in vitro were correlated with transplantability in vivo.

70-980 MEDIUM POLLUTION RATES IN CELL CULTURES. (E.) Gori, G. B. (NCI, Bethesda, Md.). J. Nat. Cancer Inst. 44(2):275-281, 1970.

Medium pollution by catabolic products (identified as dialyzable and nondialyzable factors) was studied in cultures of mycoplasma-free HEp-2 and Wistar-38 cells and in minimally contaminated cultures of HeLa S-3-1 cells. Lactic acid production was used as an index of the degree and rate of medium pollution, when correlated with tests of cloning efficiency. The rate of medium pollution depended on the type of cells, the growth conditions and the density (relative mass) of the cells in the culture, rather than on the number of cells in the culture. Several potential uses of the medium pollution rate are discussed. A mathematical model is also presented.

0-981 SPONTANEOUS NEOPLASTIC TRANSFORMATION IN VITRO: ULTRASTRUCTURE OF TRANSFORMED CELL STRAINS AND TUMORS PRODUCED BY INJECTION OF CELL STRAINS. (E.) Cornell, R. (Massachusetts Gen. Hosp., Boston). J. Nat. Cancer Inst. 43(4): 91-906, 1969.

Four spontaneously transformed cell strains (derived independently from 4 pools of C3H/HeN mouse - Albany rat embryonic cells), and cells from the tumors induced by i.m. inj. of these cell strains into non-irradiated, syngeneic hosts, were ultrastructurally closely similar to normal connective tissue fibroblasts in vivo. The interstitium from the tumors showed abundant collagen fibers and smaller non-banded filaments. The cultures also showed abundant non-banded extracellular filaments, but had fewer collagen fibers than the tumors. Virus particles were not consistently associated with either the cell cultures or the tumors induced by these cultures, though some cultures and tumors showed intrasternal A particles and both budding and extracellular C particles.

70-982 NUCLEOHISTONES. VI. COMPARATIVE STUDIES OF CHROMATIN FROM LEUKEMIC CELLS AND FROM NORMAL GRANULOCYTES. (Ger.) Drings, P. (U. Heidelberg Med. Clin., Germany) and E. Harbers. Acta Haemat. (Basel) 41(1):25-32, 1969.

The nuclei of WBC from 5 pts. with acute leukemia and 5 with chronic myeloid leukemia were fractionated and the DNA content in the euchromatin and heterochromatin fractions determined. The results were compared to values obtained from granulocytes and lymphocytes from 7 healthy subjects and 9 pts. who showed a shift to the left in their differential count. The av. DNA content/normal leukocyte was 5.4×10^{-6} μ g; leukemic cells showed no significant deviation from this value. In normal granulocytes, 53% of the DNA was in the euchromatin and 47% in the heterochromatin. Values for normal lymphocytes were 32% and 68%, resp. In young cells (shift to the left) the DNA in euchromatin was increased, in heterochromatin correspondingly decreased. Leukemic cells from all pts., with the exception of 2 with reticulosis and 1 with subacute chronic myeloid leukemia, showed a significant increase of DNA in the euchromatin fraction and corresponding decrease in the heterochromatin fraction. These results indicate that the changes leading to leukemia take place in an earlier stage of cell maturation.

70-983 SPONTANEOUS MAMMARY GLAND AND LUNG CANCERS IN C3H/W, C3H/AW, A/W AND DBA/2W MICE. (Pol.) Czarnomska, A. (Inst. Biol. Tumor Inst. Oncol., Warsaw) Nowotwory 19(2): 85-92, 1969.

Incidence and types of cancer in groups of male and multiparous, virgin and oophorectomized (oox.) females of these inbred substrains were analyzed. The greatest frequency of mammary tumors was observed in breeding females of the C3H/W strain (100% at an av. age of 331 days) followed by C3H/AW (84% at av. 387 days), DBA/2W (80% at 550 days) and A/W (43% at 425 days). The incidence among virgin animals was 93.5%, 45.7%, 67.5% and 0%, resp., at an av. age of 400, 436 and 512 days, resp. The incidence among oox. animals was 30% in C3H/W, 23.5% in C3H/AW and 5.5% in A/W at an av. age of 598, 649 and 734 days, resp. The most frequent were mammary adenocarcinomas type B (70), followed by type AB (27), A(25) and C(2). No adenoacanthomas were observed; 22 tumors remained unclassified. The greatest incidence in lung tumors was seen in A/W males (26.4%) and females (21.7%) at 423 and 425 days, resp., and greater incidence among females of C3H/AW (20%), C3H/W (18.1%) and DBA/2W (7.2%) after 492, 524 and 550 days than among males (5.5%, 8.3% and 4.1%, resp.) after 714, 573 and 175 days, resp. It is stressed that substrains of the same strain raised at different laboratories (as for instance C3H/AW and C3H/W) differ as to incidence of spontaneous tumors.

- 70-984 INITIATION OF REGENERATION IN ADULT *Rana pipiens* LIMBS BY INJECTION OF HOMOLOGOUS LIVER NUCLEAR RNP. (E.) Smith, S. D. (U. Kentucky, Lexington) and G. L. Crawford. *Oncologia (Basel)* 23(4):299-307, 1969.

In 25 surviving *Rana pipiens* with an amputated forearm, 40 daily inj. (6/week) of 0.01 ml frog liver nuclear ribonucleoprotein (RNP) into the stump stimulated limb regeneration over a 2-mo. period, as evaluated histologically. The capacity of RNP to induce regeneration was eliminated by treatment of the RNP with RNase, but not with DNase.

- 70-985 PSYCHOKINESIS IN EXPERIMENTAL TUMOR-IGENESIS. (Sp.) Elguin, G. H. (U. Chile, Santiago) and B. Onetto. *Acta Psiquiat. Psicol. Amer. Lat.* 14(1):47-60, 1968.

Three groups of 30 male and female C3H mice (aged 65-75 days at the start of the experiment) were inoc. s.c. with a suspension of transplantable C3H mammary carcinoma cells (8×10^7 cells/single dose; which produced 100% tumor takes and metastases in 71% of inoc. animals). One group served as controls; one was subjected to 20 daily, half-hour periods of intense concentration on the part of an investigator attempting to enhance tumor growth by a combination of willing and anticipating this result; one received similar treatment from an investigator attempting to retard tumor growth. As determined by measurements of the tumors on days 16 and 22, resp., determination of tumor wts. and vols. after sacrifice on day 23, etc., no significant differences appeared between the control group and the one for which enhancement of tumor growth was attempted. However, as compared to the other 2 groups, tumor growth was significantly retarded in the group for which such retardation was attempted and total body wts. were significantly greater at the time of sacrifice, all animals in the other groups having experienced a significant wt. loss.

- 70-986 CARCINOMA OF THE CERVIX: DEFICIENCY OF NEXUS INTERCELLULAR JUNCTIONS. (E.) McNutt, N. S. (Massachusetts Gen. Hosp. Path. Lab., Boston) and R. S. Weinstein. *Science* 165(3893):597-599, 1969.

Thin sections of 5 normal specimens of the cervical epithelium and 4 invasive squamous cell carcinomas of the cervix (treated with colloidal lanthanum hydroxide for negative staining of the extracellular spaces) were examined under the electron microscope. Normal cervical epithelium showed numerous areas where the membranes of adjacent cells were about 20 Å apart (nexuses). Two of the tumors had no nexuses at all; the other 2 tumors showed an occasional nexus. In

the normal epithelium, as many as 4 nexuses, connecting interdigitating microvilli of adjacent cells, were noted. Similar patterns were occasionally seen in histologically well-differentiated regions of the 2 tumors which showed any nexuses, but not in the less differentiated regions of any of the tumors. It is suggested that a deficiency of these intercellular nexuses may be related to the invasive property of tumor growth.

- 70-987 NON-NEOPLASTIC SURFACE EPITHELIUM CONTINUOUS WITH INVASIVE CERVICAL CARCINOMA. (E.) Grubb, C. (Roy. Free Hosp., London) and I. Janota. *Neoplasma (Bratisl.)* 16(2):215-221, 1969.

The histologic picture, observed in punch biopsies of 5 pts., supported the suggestion that invasive cervical carcinoma may arise from the deep layers of a surface epithelium not replaced by intraepithelial carcinoma.

- 70-988 MORPHOLOGIC DEFINITION OF ULCUS TEREBRANS AS A FORM OF BASALIOMA. (Ger.) Kleemann, W. (Karl Marx U. Derm. Clin., Leipzig, Germany). *Derm. Wschr.* 154(51):1203-1211, 1968.

Between 1962-1966, inclusive, a university dermatologic clinic saw 1722 cases of benign or transitional basocellular tumors 253 of spinalioma, 159 of basal cell carcinoma, and only 3 of ulcer terebrans. Morphological and histological studies of these 3, and a fourth pt. treated from 1948-1959, confirmed that all 4 were properly classified as infiltrating, destructive basal cell carcinomas (so-called metatypical basocellular epitheliomas), developing relatively suddenly out of semimalignant rodent ulcers, due to unknown influences. Recurrences, especially after X-ray therapy, appeared in the form of mixed tumors, containing strands of solid, basaliomatous cells with peripheral cells organized into palisades, mixed with cells which were rich in protoplasm and which tended to be ranged concentrically around parakeratotic horn cells.

- 70-989 BUCCAL SEX-CHROMATIN AND BREAST CANCER. (E.) Yule, R. (Christie Hosp., Manchester, England), M. Howell and B. Verrill. *Lancet* 2(7625):824-825, 1969.

The mean Barr-Body count in buccal smears from normal control women, women with cervical cancer and women with breast cancer did not differ significantly, based on a one-way analysis of variance. This laboratory test would form a poor basis for a selective screening procedure to detect those at risk of developing breast cancer.

See also abstract no.: 594

AUTHOR INDEX

- aronson, S. A. 812,851
 chord, J. L. 962
 ckerman, E. 940
 kasu, F. 967
 kimova, R. N. 726
 hl, R. 752
 Aleksandrowicz, J. 916
 Alexandrov, V. A. 713
 l-Falluji, M. 864
 lford, T. 838
 lligaier, C. 789
 llison, A. C. 875,876
 mbrose, K. R. 845
 mes, R. P. 822
 nderson, C. K. 922
 nderson, D. L. 895
 nderson, J. 833
 nderson, N. G. 845
 oki, T. 873
 ppelgren, K. L. 974
 raki, M. 616
 rcher, F. L. 938
 rseculeratne, S. N. 670
 shley, D. J. B. 896,904
 shley, L. M. 666
 shmeade-Dyer, A. 884
 vrameas, S. 849

 aba, S. 739,743
 ader, A. V. 809
 arwald, R. J. 625
 ingana, N. 878
 aker, R. S. U. 810
 lasubramaniam, K. 670
 ill, J. K. 614
 ilslev, I. 898
 inks, K. W. 722
 inna, M. 965
 rber, H. R. K. 557
 rker, B. E. 977
 roche, C. 626
 ron, J. 646
 ron, S. 843
 rrick, S. 868
 rtle, K. D. 599
 ther, R. 803
 uer, H. 789
 xendale, W. 832
 ard, D. 779
 ard, J. W. 778,779
 icker, Y. 831
 abehani, A. M. 868
 ell, J. R. 690
 Etzelzen, P. 818
 Enhard, W. 849
 E gol'ts, V. M. 578
 E gs, M. 759
 E gs, V. V. 759
 E si, M. 954
 B talanffy, F. D. 920
 B ving, L. J. 708,709
 B radwaj, V. P. 695
 B de, S. V. 621,660

 Biava, C. G. 573
 Bigner, D. D. 797
 Bird, E. S. 704
 Björklund, B. 751
 Blackstein, M. E. 861
 Bloch, D. A. 931
 Blunck, J. M. 651
 Boeryd, B. 622
 Boiron, M. 805,807
 Bolano, C. R. 868
 Bolognese, R. J. 907
 Bolognesi, D. P. 779
 Bonneau, H. 856,862
 Bopp, W. J. 756
 Borsos, T. 654,655,656
 Bösenberg, H. 663,664
 Bournali, M.-F. 853
 Bourse, R. 734
 Boush, G. M. 625
 Boyce, W. H. 722
 Brada, Z. 754
 Bradshaw, E. 901,928
 Bras, G. 884
 Braun, A. 653
 Brioux de Salum, S. 978
 Brill, E. 738
 Brisou, J. 601
 Brown, G. B. 618
 Brown, M. M. 558
 Bruce, D. L. 888
 Bubenék, J. 789
 Buck, B. M. 803
 Buncher, C. R. 930
 Bunnag, B. 838
 Burki, H. R. 649
 Burkitt, D. P. 885
 Burney, S. W. 690
 Burroughs, M. A. K. 824
 Buu-Hoi, N. P. 619

 Cacciari, P. 707
 Caiafa, P. 976
 Calafat, J. 816,818
 Came, P. E. 823
 Camerini, E. 628
 Cameron, L. 889
 Campbell, T. C. 750
 Campobasso, O. 724
 Candeli, A. 603
 Canepari, C. 683
 Canivet, M. 805
 Cardini, G. 954
 Carretti, D. 683
 Carter, R. L. 606,607
 Cascinelli, N. 913
 Cassai, E. 863
 Cassingena, R. 853
 Casto, B. C. 844
 Ceglowski, W. S. 765
 Cesarini, J. P. 862
 Chakrabarty, A. K. 765
 Chapman, A. L. 756
 Charney, J. 822

 Charuzy, I. 696
 Chatelin, C. L. 596
 Chou, M. W. 740
 Chouroulinkov, I. 732
 Chubb, R. C. 832
 Chung, M. 785
 Churchill, A. E. 832
 Churchill, W. H., Jr. 655
 Churg, J. 679
 Citoler, P. 633
 Clademenos, T. 661
 Clark, W. R. 840,841
 Clarkson, B. D. 921
 Clausen, K. P. 949
 Clayson, D. B. 724
 Clemente, R. 954
 Clemmesen, J. 574,936
 Clifford, J. I. 667
 Clifford, P. 826,827,828
 Codegone, M. L. 665
 Coggin, J. H., Jr. 845,846
 Cohen, H. 756
 Cohen, M. H. 773
 Cole, H. 884
 Colnaghi, M. E. 608
 Consigli, R. A. 860
 Cook, M. K. 877
 Cooke, R. A. 693
 Cooper, E. H. 922
 Cornell, R. 981
 Corson, S. L. 907
 Cosgrove, G. E. 589
 Court Brown, W. M. 952
 Cowen, D. M. 724
 Cox, C. E. 722
 Cox, D. E. 918
 Crawford, G. L. 984
 Cremer, N. E. 768
 Croisy-Delcey, M. 619
 Cuq, J.-P. 961
 Cure, S. F. 768
 Cusumano, C. 838
 Czarnomska, A. 983

 Daftary, D. K. 935
 Dagle, G. E. 841
 D'Alonzo, U. 964
 Dao, T. L. 711
 Daudel, P. 619
 Davey, D. A. 908
 Davies, R. F. 688
 Davis, W. C. 963
 Davison, B. C. C. 886
 Dawson, P. J. 769,771
 Day, E. D. 797
 Day, T. D. 688
 DeBaun, J. R. 672
 Debray, C. 961
 Debski, T. 916
 Defendi, V. 867
 Dehnen, W. 643
 De Jager, H. 681
 Della Porta, G. 608

- Delwaide, P. A. 640,641
 Dent, P. B. 763
 DeOme, K. B. 710,819
 Detroy, R. W. 662
 de Vaux Saint Cyr, C. 848
 DeVita, V. T. 959
 De Waard, F. 583
 Diggelmann, H. 794
 Dillingham, L. A. 700
 Diringer, H. 698
 Dmochowski, L. 811
 Dodd, M. C. 864
 Dodo, H. 931
 Dontenwill, W. 675,687
 Dorn, C. R. 969
 Dougherty, R. M. 777
 Dourmashkin, R. 786
 Drings, P. 982
 Drozdová, A. 754
 Druckrey, H. 637
 Dubbs, D. R. 852
 Duff, R. G. 781
 Dunkel, V. C. 829
 Dunn, G. R. 957
 Dunn, T. B. 715
 Dutrillaux, M.-C. 817
 Dzhiyev, F. K. 724
- Easton, J. M. 958
 Ebbesen, P. 973
 Eckenhoff, J. E. 888
 Eckhart, W. 580
 Edward, V. D. 692
 Edwards, L. D. 733
 Eide, K. A. 888
 Eisenberg, H. 909
 Eisenstein, S. 759
 Eisenstein, Z. 883
 Elguin, G. H. 985
 Elliott, S. C. 617
 Elmenhorst, H. 675
 Elrod, L. H. 845
 Epstein, S. M. 671
 Eshleman, L. 885
 Estrade, S. 853
 Étienne, J.-P. 961
- Fábíán, B. 604
 Faed, M. J. W. 956
 Falor, W. H. 684
 Farber, E. 671
 Farmilo, A. J. 861
 Farooki, M. A. 584
 Faulkin, L. J., Jr. 819
 Fefer, A. 808
 Fehr, P. M. 572
 Ferreira-Salgado, M.-A. 857
 Fiala, A. E. 652
 Fiala, S. 652
 Fieldsteel, A. H. 769,771
 Filippov, A. I. 942
 Fink, M. A. 773
 Fischinger, P. J. 806
 Fitzgerald, P. H. 934
- Fletcher, C. M. 737
 Fogh, J. 847
 Fondarai, J. 856
 Forni, A. 951
 Förström, L. 595
 Fort, L. 971
 Foster, J. A. 627
 Foy, H. 970
 Fraumeni, J. F., Jr. 585,586,
 914,926,933,958,959
 Fredrickson, T. N. 870
 Freeman, A. E. 776
 Fried, J. 921
 Friedell, G. H. 690
 Friedman, H. 765,766,767
 Friedmann, I. 568,704
 Fritsch, S. 813
 Fritz, R. B. 778,779,797
 Fujinaga, K. 835
 Furuya, M. 613
- Gadrat, J. 734
 Gaffney, E. V. 847
 Galetti, G. 730
 Gangolli, S. D. 699
 Gantt, R. C. 931
 Garcia, H. 712
 Gargus, J. L. 676,701
 Gelboin, H. V. 685
 Gentile, A. 581
 Georgii, A. 866
 Gerke, G. 663
 Ghetti, G. 683
 Ghittino, P. 665
 Gichner, T. 741
 Gilden, R. 802
 Gilden, R. V. 801
 Giri, C. P. 621
 Gogichadze, G. K. 579
 Goldberg, M. L. 950
 Goldé, A. 784
 Goldenberg, H. 938
 Goldner, H. 767
 Goldstein, D. P. 947
 Goldstein, G. 826
 Good, R. A. 763
 Gordon, M. 684
 Gori, G. B. 980
 Gothoskar, S. V. 660
 Gotlieb-Stematsky, T. 979
 Grabar, P. 848
 Graber, E. A. 557
 Graf, T. 789
 Grant, G. A. 611,702,703
 Grasso, P. 609,699
 Green, B. 747
 Green, M. 835
 Greenberg, R. A. 909
 Greenlaw, R. H. 588
 Gross, K. 911
 Grosse, H. 891
 Groth, D. H. 678
 Grubb, C. 987
 Grunberg, E. 605
 Guérin, M. 732
- Guerrero, A. 712
 Guillemain, B. 807
 Guillon, J.-C. 732
 Gupta, P. C. 935
 Gupta, P. K. 705
 Gusek, W. 719
- Hageman, P. 816
 Hageman, P. C. 818
 Hågerstrand, I. 966
 Hagmar, B. 622
 Haguenau, F. 787
 Hall, W. T. 815
 Halver, J. E. 666
 Hamer, J. W. 934
 Hamilton, P. B. 749
 Hammond, E. C. 900
 Hampar, B. 824
 Hampe, A. 807
 Hampton, S. 798
 Harbers, E. 982
 Harke, H.-P. 675,687
 Harnden, D. G. 952,956
 Harrison, L. H. 722
 Hay, D. 760
 Heath, C. W., Jr. 917
 Heidelberger, C. 698
 Heine, U. 779
 Heinecke, H. 813
 Helmboldt, C. F. 870
 Henle, G. 826,827
 Henle, W. 826,827
 Henry, M. 817
 Heppner, G. H. 820,821
 Herberman, R. B. 855
 Herbet, A. 848
 Herz, A. 761
 Herzog, L. 866
 Hesseltine, C. W. 662
 Hilf, R. 938
 Hilleman, M. R. 840,841,842
 Hinz, R. W. 785
 Hirano, S. 766
 Hirsch, M. S. 875,876
 Hirschman, S. Z. 806
 Hollande, E. 817
 Hollinshead, A. 838
 Holmes, E. C. 657
 Holtz, J. L. 678
 Homer, R. B. 747
 Hooson, J. 699
 Horsch, A. 972
 Hosokawa, A. 613
 Hosokawa, M. 764
 Howe, C. D. 869
 Howell, M. 989
 Hrushovetz, S. B. 894
 Huebner, R. J. 557,776,802,
 814,843,919
 Hurst, L. 650
 Hyman, G. A. 882
- Igel, H. J. 776
 Iijima, S. 930

- Imamura, A. 598
 Inomata, M. 598
 Invernizzi, F. 730
 Ioki, Y. 598
 Iorio, A. M. 865
 Isard, H. J. 912
 Ishimoto, A. 774
 Ito, Y. 925
 Ivankovic, S. 637,723
 Ivanova, N. A. 793,800
 Iwahara, S. 739
 Iwakami, T. 967
 Iwameji, Y. 872
 Iwao, M. 739
 Izzotti, S. 905

 Jaccox, H. W. 593
 Jacquignon, P. 619
 Janisch, W. 631,632
 Janota, I. 987
 Jarrett, O. 760
 Jasmin, G. 725
 Jasty, V. 833
 Jenkins, D. C. 756
 Jensen, H.-E. 898
 Joffe, A. Z. 669
 Jones, D. W. 599
 Jungst, W. 813

 Juczala, O. A. 684
 Jufuko, G. W. 878
 Khan, B. D. 657
 Kaji, H. 764
 Kajima, M. 575,731,790
 Kaliev, Y. 850
 Kalner, G. 879
 Kamada, N. 590,591,592
 Kaneuchi, C. 620
 Kanono, T. 597
 Kaplan, L. 960
 Karra, J. 874
 Katinová, L. 874
 Kato, M. 946
 Kato, R. 642
 Kato, T. 946
 Katsnel'son, B. A. 736
 Katsuta, H. 613
 Katsumura, A., Jr. 925
 Kashima, K. 946
 Kazoe, Y. 616
 Keller, H.-P. 834
 Kellhoff, G. 802
 Kellhoff, G. J. 814
 Kelly, R. E. 929
 Kerdrey, G. 629
 Kestring, G. 634
 Ketsch, C. R. 930
 Ketsch, F. M. 940
 Ketsch, W. K. 617
 Ketsch, W. H. 753
 Ketsch, S. 852
 Katabatake, T. 561
 Kassen, C. H. L. 681
 Ketschmann, W. 988

 Kleihues, P. 630,635
 Klein, G. 770,826,
 827,828,945
 Knight, E. M. 878
 Kobayashi, H. 764
 Kodama, T. 764
 Koike, N. 946
 Kondi, A. 970
 Kononova, V. A. 735
 Kordač, V. 653
 Koss, L. G. 929
 Kosuge, T. 744
 Kothari, M. L. 587
 Kroes, R. 720
 Kronman, B. S. 655,656
 Kurahara, C. 769,771
 Kurita, Y. 729
 Kurland, L. T. 887
 Kurokawa, S. 561
 Kuwabara, S. 967
 Kwa, H. G. 727,728
 Kwon, E. H. 944

 Lacassagne, A. 650
 Lahiri, V. L. 695
 Laing, D. 825
 Laird, H. M. 760
 Lake, B. 892
 Lamb, E. J. 947
 Landschütz, C. 637
 Lane, W. T. 814
 Langlands, A. O. 956
 Langlois, A. J. 779
 Larsen, W. E. 756
 Larson, V. M. 840,841,842
 Lasfargues, E. Y. 822
 Laub, M. 943
 Lavenda, N. 783
 Law, L. W. 755,804
 Leclerc, J. C. 762
 Leduc, E. H. 849
 Lee, A. M. 926
 Lee, Y. K. 802
 Lehman, J. M. 867
 Lehmann, G. 644
 Lehnert, G. 686
 Leighton, J. 671
 Lestchinskaya, N. P. 793,800
 Letourneux, M. 972
 Levi, P. E. 922
 Levij, I. S. 694,696
 Levinson, W. 795
 Levy, B. M. 798
 Levy, J. A. 757
 Levy, J. P. 762
 Lewis, A. C. W. 886
 Ley, H. L. 573
 Leymarios, J. 961
 Li, F. P. 914,933
 Linde, H. W. 888
 Linsell, C. A. 970
 Ljungberg, O. 948
 Log, T. 801
 Louis, C. J. 651
 Luschnitz, E. 834

 Lutchter, F. 619
 Luthra, U. K. 695

 Maamies, T. J. 903
 Mackie, B. S. 691
 Madden, G. E. 678
 Maeda, M. 774
 Mahmoud, I. Y. 783
 Malinin, G. I. 839
 Mallett, L. 600
 Malmgren, R. A. 815
 Maltoni, C. 683
 Mancini, L. O. 833
 Mancuso, T. F. 902
 Manocha, S. L. 923
 Mantel, N. 933
 Marhold, J. 571,648,746
 Mariani, T. 763
 Marková, H. 911
 Martínez, I. 932
 Maruyama, Y. 940
 Maryak, J. M. 776
 Mashelkar, B. N. 615
 Maškillejson, A. L. 594
 Małernowska, W. 682
 Matoška, J. 799
 Matrká, M. 571,648,746
 Matsumoto, S. 635
 Matthews, R. S. 599
 May, E. 853
 Mayer, L. A. 753
 McBeath, S. 956
 McConahey, W. M. 887
 McCormick, K. J. 828
 McDonough, G. R. 747
 McGovern, V. J. 558
 McNutt, N. S. 986
 McPhedran, P. 917
 Medina, D. 710,819
 Mehta, F. S. 935
 Mehta, L. A. 587
 Meier, H. 919
 Meimamed, M. R. 929
 Mellors, R. C. 871
 Melzer, M. S. 612
 Merkow, L. P. 671
 Merrill, J. A. 906
 Meyer, G. 856
 Michelson-Fiske, S. 787
 Miller, E. C. 672
 Miller, J. A. 672
 Miller, R. W. 890,933
 Miller, S. V. 736
 Minton, J. P. 864
 Mishima, Y. 968
 Mitchley, B. C. V. 607
 Miyata, M. 613
 Mizutani, T. 620
 Modan, B. 883
 Modová, B. 976
 Monnier, J. 734
 Montagnier, L. 784
 Moore, D. H. 822,823
 Moore, O. S. 931
 Mordell, J. S. 902

- Moreau, J. 619
 Moreo, L. 951
 Mori, Y. 739
 Morioka, S. 968
 Morozzi, G. 603
 Morton, D. L. 657,815
 Mukerji, B. 716
 Mulay, A. S. 674
 Müller, E. 602
 Munn, A. 924
 Munn, R. J. 761
 Murphy, P. J. 645
 Mussgay, M. 752
 Myers, D. D. 919
- Nadkarni, J. J. 828
 Nadkarni, J. S. 828
 Nagata, C. 598
 Nánássi, E. 943
 Nebert, D. W. 647,685
 Neunhoeffter, O. 644
 Newton-Howes, J. S. 737
 Nielsen, A. H. 756
 Nielsen, J. 898
 Nishizuka, Y. 729
 Nobrega, F. T. 887
- O'Connor, T. E. 806
 Oettgen, H. F. 945
 O'Gara, R. W. 674
 Ogawa, M. 921
 Ogino, T. 836
 Ohta, S. 613
 Okano, T. 597,745
 Okita, G. T. 649
 Olansky, S. 962
 Oleinick, A. 880
 Olinici, C. 560
 Olson, R. O., Jr. 963
 Onetto, B. 985
 Oppenheim, E. 762
 O'Riordan, M. 956
 Orlando, R. A. 938
 O'Rourke, J. J. 557
 Oser, B. L. 573
 Oshima, T. 642
 Osske, G. 631
 Ostrum, B. J. 912
 Otto, H. 680
 Owen, R. 937
 Oyamada, Y. 743
- Palestro, G. 721
 Panteleakis, P. N. 842
 Pardo, M. 671
 Parker, A. M. 970
 Parks, R. C. 755
 Parmiani, G. 608
 Parwani, G. S. 965
 Pattee, H. E. 748
 Paupe, J. 565
 Pavlovsky, A. 978
 Pavlovsky, S. 978
- Paynter, O. E. 701
 Pearson, G. 826,827
 Pepper, S. S. 810
 Peries, J. 805
 Perry, J. L. 860
 Peterson, H.-I. 974
 Pilgrim, H. I. 755
 Pindborg, J. J. 935
 Pinn, V. M. 705
 Pípalová, J. 648
 Pirogov, N. I. 953
 Pitzurra, M. 865
 Plowman, K. M. 750
 Pliznik, D. H. 975
 Pokorný, V. 741
 Pollard, M. 790
 Polliack, A. 694,696
 Popnikolov, V. S. 953
 Portman, R. S. 750
 Prechtel, K. 866
 Preda, F. 913
 Prehn, R. T. 700
 Pressman, D. 770
 Price, J. M. 570,573
 Price, P. J. 776
 Prince, H. N. 605
 Prince, W. R. 749
 Pris, J. 734
 Provana, A. 665
 Purchase, I. F. H. 668
 Pyrah, L. N. 562
- Rabinowitz, Z. 858,859
 Rabotti, G. 758
 Rabotti, G. F. 787
 Rambousek, V. 571,648
 Rapp, H. J. 654,655,656
 Rask-Nielsen, R. 973
 Ravich, A. 576
 Reckzeh, G. 675,687
 Reczko, E. 752
 Reddy, D. B. 692
 Reddy, D. G. 692
 Rees, K. R. 667
 Reese, W. H., Jr. 676,701
 Reichert, J. K. 602
 Reid, B. L. 706
 Reilly, C. A., Jr. 617
 Reiner, J. 658
 Reuber, M. D. 673
 Ribacchi, R. 677
 Riopelle, J. L. 725
 Robertson, D. G. 737
 Roche, J. G. 950
 Roe, F. J. C. 606,607,611, 629,702,703
 Rondia, D. 640
 Rosenau, W. 950
 Rosengren, B. H. O. 974
 Rossi Fanelli, A. 976
 Roth, F. K. 777
 Rothwell, K. 689
 Ruà, S. 721
 Rubin, H. 791
 Rubin, R. C. 822
- Rucker, K. 687
 Rudali, G. 718
 Ruffer, F. 571
 Ruibal, B. 978
 Rutter, H. A. 676
 Rwomushana, J. W. 694
- Sachs, L. 858,859
 Sahu, A. B. 716
 Saint-Martin, J. 565
 Saito, H. 764
 Salomon, J.-C. 972
 Sampson, R. J. 930
 Sander, J. 639
 Sanford, K. K. 977
 Sapre, N. N. 660
 Saraste, K. 903
 Sarkar, N. H. 822
 Sarma, P. S. 801,843
 Sato, Y. 745
 Sawanishi, H. 744
 Schagholi, H. 643
 Schaller, K.-H. 686
 Schalm, O. W. 761
 Schidlovsky, G. 815
 Schiffer, Z. 916
 Schlee, D. 567
 Schloss, G. T. 617
 Schmöhl, D. 717
 Schneider, R. 969
 Schoenberg, B. S. 909
 Schön, E. 653
 Schönebeck, J. 966
 Schonland, M. 901,928
 Schultze, H. 686
 Schwaier, R. 742
 Sears, J. F. 877
 Seidel, H. J. 775
 Seif, F. 639
 Sendo, F. 764
 Senyszyn, J. J. 593
 Sessa, A. 730
 Shabad, L. M. 714
 Shaffer, W. L. 906
 Sherwood, K. K. 893
 Shilo, R. 912
 Shimojo, H. 837
 Shirai, T. 764
 Shirasu, Y. 620
 Shirodkar, A. S. 615
 Shiu, G. 843
 Simkovic, D. 796
 Simons, P. J. 810
 Simu, G. 560
 Sinha, D. 716
 Sinkovics, J. G. 869
 Sizaret, P. 970
 Skinner, E. F. 569
 Slifkin, M. 671
 Słomska, J. 910
 Smida, J. 792,799
 Smidová, V. 792,799
 Smith, J. W. 749
 Smith, J. Y. R. 672
 Smith, L. H. 623

Smith, M. V. A. 758
 Smith, P. G. 952
 Smith, R. R. 666
 Smith, S. D. 984
 Morodintzev, A. A. 793,800
 So, B. T. 638
 Sobczak, E. 848
 Soehner, R. L. 811
 Sorokin, E. 566
 Soto, E. 690
 Southam, C. M. 658
 Szvári, M. 943
 Tachura, J. 682
 Tadler, L. 675
 Tanners, C. P. 861
 Taszewski, J. 897
 Tavrou, D. 636
 Teele, H. D. 923
 Teinfeld, J. 573
 Teinmuller, D. 700
 Tenback, W. A. 828
 Těrbá, S. 911
 Tern, B. D. 960
 Tevens, L. C. 957
 Tewart, A. 559
 Teyn, M. 668
 Tich, H. F. 923
 Thirer, G. 618
 Thokinger, H. E. 678
 Trom, R. 976
 Tráez, H. G. 978
 Tsiyama, T. 729
 Tmitani, J. 967
 Ttherland, D. J. 624
 Tzuki, H. 743
 Tzuki, K. 946
 Tzuki, Y. 679,774
 Tz, J. 796
 Tzoboda, J. 786
 Tzoboda, V. 881
 Tzen, G. J. V. 772
 Tzdkowski, D. 686
 Tz, P. D. 705
 Tzadate, A. 597
 Tzahashi, A. 642
 Tzahashi, M. 836
 Tzahashi, T. 925
 Tzaka, T. 613
 Tzatsuki, K. 915
 Tzeichi, N. 764
 Tzenaka, S. 745
 Tza, P. 903
 Tzooka, H. 616
 Tzer, H. S. 971
 Tzchnitz, C. 834
 Tzor, A. C. 798
 Tzor, D. O. N. 969
 Tzekoon, G. E. 670
 Tzily, T. R. 646
 Tzi, M. 863

Terracini, B. 721
 Thatcher, F. S. 661
 Theilen, G. H. 761
 Theologides, A. 941
 Thewlis, B. H. 610
 Thoma, G. W. 798
 Thomas, C. 633,634,638
 Thomas, J. A. 817
 Thust, R. 632
 Tibemanya, J. 878
 Timmermans, A. 818
 Ting, R. C. 804,809,855
 Tissier, M. 600
 Tobe, T. 946
 Tobiška, J. 754
 Todaro, G. J. 812,851
 Tomingas, R. 643
 Toni, R. 802
 Tough, I. M. 952
 Tournier, P. 853
 Toyoshima, K. 782
 Trentin, J. J. 828
 Trevisio, A. 721
 Tu, S.-M. 925
 Tung, T. C. 740
 Turner, H. C. 814

Ujházy, V. 799
 Ungar, H. 669

v. Fragstein, J. G. 680
 Vaittinen, E. 899
 Valladares, Y. 577
 van der Gugten, A. A. 727,728
 Van Esch, G. J. 720
 Van Frank, R. M. 645
 van Gorp, L. H. M. 772
 Van Persijn Van Meerten, O. H. 681
 van Walbeek, W. 661
 Varela-Nunez, R. 955
 Varet, B. 762
 Velemínský, J. 741
 Velichkovskii, B. T. 736
 Verby, J. E. 887
 Verhofstad, F. 727,728
 Veronesi, U. 913
 Verrill, B. 989
 Veys, C. A. 927
 Vigier, P. 784
 Vilain, C. 817
 Virag, I. 883
 Vogel, C. L. 958,959
 Vogin, E. E. 573
 Vogt, P. K. 781,782
 Von Haam, E. 949
 Vonka, V. 874
 von Studnitz, W. 948

Wagner, W. D. 678
 Wahi, P. N. 695
 Wakabayashi, A. 788
 Walburg, H. E., Jr. 589
 Warrell, D. A. 737
 Warzok, R. 631
 Watler, D. C. 884
 Wechsler, W. 635
 Weinberg, A. 831
 Weinstein, R. S. 986
 Weiss, D. W. 820,821
 Weissmann, C. 794
 Wepsic, H. T. 654,655
 Werder, A. A. 756
 Whang-Peng, J. 654
 Whitehead, J. K. 689
 Wicker, R. 848,849
 Wijesundera, S. 670
 Wilhelm, G. 644
 Williams, E. H. 885
 Williams, R. E. 922
 Williams, T. L. 645
 Winker, J. 685
 Witz, I. 770
 Wood, M. 724
 Wood, P. C. 820,821
 Wolfová, H. 911
 Woodruff, M. 623
 Woods, D. A. 697
 Woolner, L. B. 887
 Wynder, E. L. 582,931

Yamagiwa, H. 939
 Yamaguchi, J. 830
 Yamamoto, S. 620
 Yamashita, T. 837
 Yaniv, A. 979
 Yates, V. J. 833
 Yatoimi, K. 946
 Yokota, M. 744
 Yoneyama, T. 588
 Yoshida, T. 659
 Young, J. C. 776
 Young, L. 710
 Zule, R. 989
 Zacharia, T. P. 790
 Zaki, G. F. 941
 Zamfiresco, M. 854
 Závada, J. 780
 Závadová, H. 874
 Zavanella, T. 628
 Zbar, B. 654,655
 Zeigel, R. F. 758,829
 Zenda, H. 744
 Zironi, A. 563,564
 Zisman, B. 875,876
 Zobl, H. 866
 Zotikov, L. A. 726
 Zuelzer, W. W. 918
 Zülch, K. J. 635

SUBJECT INDEX

ABSORPTION

- benzpyrene, lung, hamster: 675
- dimethylbenzanthracene, lung, hamster: 675

ACETAMIDE, THIO-

- organ-specific effect on liver glycogen, mouse: 660

ACETYLAMINOFLUORENE (See N-2-Fluorenylacetamide)

ACTINOMYCIN D (See under Antitumor agents)

ADRENAL NEOPLASMS

- pheochromocytoma (epinephrine-producing), with medullary carcinoma of thyroid, familial: 948

AFLATOXIN(S)

- biosynthesis
 - Aspergillus culture on tobacco: 748
 - effect of refrigeration, Aspergillus flavus: 661
- cyclopropenes, toxicity, liver, trout: 665
- dietary, toxicity, farm animals, review: 572
- effect on
 - connective tissue, rat: 699
 - lysosomes, rat liver: 670
- fluorescent derivatives (from UV-irradiated preparation or biological materials), analysis, method: 664
- isolation and purification, method: 663
- toxicity
 - lung, mouse: 701
 - role of salmonellosis, chicken: 749
 - species difference, mechanism: 750

AFLATOXIN B1

- DNA binding, mechanism, cell-free system: 667
- effect on lysosomes, rat liver: 670
- excretion, rat: 740
- liver toxicity or hepatoma, species difference, salmon or trout: 666
- metabolism, sex difference, rat: 668
- steroid-hydroxylating fungi: 662
- pre malignant liver nodules, in vitro growth rate, rat: 671
- toxicity
 - rat: 740
 - skin, rabbit: 669

AFLATOXIN B2

- toxicity, skin, rabbit: 669

AFLATOXIN G1

- effect on lysosomes, rat liver: 670
- toxicity, skin, rabbit: 669

AGE FACTORS

- benzene-induced chromosome abnormalities: 952
- benzpyrene metabolism, liver microsomes, rat: 643
- cancer epidemiology, children and adolescents, U.S.: 890
- herpesvirus resistance, role of macrophages, mouse: 876
- host immunity, high-plasma cell tumor mouse strain: 973

AIR POLLUTION

- automobile exhaust, USSR (rural): 735
- lung cancer
 - proposed studies of community health: 902
 - review: 574
- polycyclic aromatic hydrocarbons, detection method: 603

AMINES

- arylhydroxylamines, oxidation to nitroso derivatives, method: 738

AMINES, AROMATIC

- carcinogenic or noncarcinogenic, free radical formation, organic solvents or water: 598

AMINOPTERIN (See under Antitumor agents)

ANESTHETICS

- occupational exposure, cancer incidence, U.S. and Canada: 888

ANTHRACENE, 9-BROMOMETHYL-

- effect on DNA, normal cells: 619

ANTIBIOTICS

- rifampicin, effect on Rous sarcoma virus production and transformation, chick embryo cells: 794

ANTILYMPHOCYTE SERUM (See under Immunosuppression)

ANTITUMOR AGENTS

- actinomycin D
 - effect on
 - avian leukosis-sarcoma or fowl plague virus, role of cellular DNA, chick or hamster embryo cells: 780
 - Moloney sarcoma virus transformation, mouse embryo cells: 803
- aminopterin, mutagenesis and effect on tumor incidence, *Drosophila*: 626
- 5-bis(2-chloroethyl)amino-6-methyluracil (thymine alkylamine), effect on Rous sarcoma virus-transformed rat cells: 796
- cyclophosphamide, effect on Moloney virus-induced sarcoma, mouse: 808
- iododeoxyuridine, effect on SV40 transformation efficiency, hamster embryo cells: 846
- mitomycin C, effect on Moloney sarcoma virus transformation, mouse embryo cells: 803
- nitrogen mustard, lung tumors, mouse: 701
- procarbazine (ibenzmethylin), lung or s.c. tumors, animal: 605

ARSENIC

- occupational exposure, respiratory cancer, U.S.: 926

ASBESTOS

- needles, detection in lung, occupational asbestos or dust exposure: 680
- occupational exposure, pleural and peritoneal mesothelioma: 681
- structure and development of asbestos bodies, lung, hamster: 679

ASCARIDOLE

- effect on DNase-II, cell-free system: 612

AZATHIOPRINE

- cervical dysplasia, human: 705

AZO DYES

- tritiated, synthesis: 739

AZOANILINE, N,N-DIMETHYL-P-PHENYL-

- toxicity, insect (cockroach): 624

AZOBENZENE DERIVATIVES

- structure-activity relationships, review: 571

AZOBENZENE, o-AMINO-

- effect on dimethylaminoazobenzene hepatoma, rat: 659

AZOBENZENE, N,N-DIMETHYL-4-AMINO-

- oxidation, cerium(IV) sulfate: 746

- AZOBENZENE, 4-DIMETHYLAMINO-
 effect on normal, transformed or neoplastic
 rat or mouse cells: 613
 hepatoma (rat)
 effect of dimethylbenzanthracene: 650
 growth rate: 920
 host factors: 659
 4'-substituted derivatives, biliary metabolites,
 rat: 648
- AZOBENZENE, 3'-METHYL-4-DIMETHYLAMINO
 hepatoma
 glutathionase activation, rat: 652
 soluble liver proteins, rat: 651
- BACTERIA
 anaerobic, benzpyrene synthesis, culture media:
 601
 soil samples: 600
- BENZ(a)ANTHRACENE
 effect on enzymes, hamster embryo cells: 647
 tumor induction, planaria: 627
- BENZANTHRACENE, 7-BROMOMETHYL-
 effect on DNA, normal cells: 619
- BENZANTHRACENE, 1:2,5:6-DI-
 binding, skin proteins, metabolite, mouse:
 698
- BENZANTHRACENE, 7,12-DIMETHYL-
 absorption, lung, hamster: 675
 cheek pouch tumors (hamster)
 effect of
 antilymphocyte serum: 697
 vitamin A: 694
 hormone effects: 696
 succinate dehydrogenase activity: 695
 effect on chromosomes, leukemic or preleukemic
 rat bone marrow: 729
 hepatoma
 effect of dimethylaminoazobenzene, rat:
 650
 germ-free mice: 611,702
 immunosuppression, newborn or adult mouse:
 614
 inhibition of Friend virus leukemia, mouse:
 617
 lung tumors, germ-free mice: 702,703
 lymphoma, germ-free mice: 731
 mammary tumors (rat): 711
 effect of oophorectomy on formation and
 maintenance of premalignant nodules: 708
 growth rate: 920
 histochemistry: 938
 hyperplastic nodules, response to growth-
 regulatory mechanisms: 709
 ovary and mammary tumors, glucose oxidation,
 mouse: 649
 s.c. sarcoma, germ-free mice: 611
 transplacental lung or kidney carcinogenesis,
 mouse: 714
- ,2-BENZANTHRACENE, 6,9,10-TRIMETHYL-
 brain tumors, DNA and histone content and
 chromosomes, rat: 632
- ENZENE
 occupational exposure
 erythroleukemia, chromosomes: 951
 WBC chromosome abnormalities, age factors:
 952
- BENZENE, DODECYL-
 toxicity, lung, mouse: 701
- BENZIDINE, 3,3'-DICHLORO-
 transplacental lung or kidney carcinogenesis,
 mouse: 714
- 3,4-BENZOPYRENE
 abnormal cellular responses, insect (cockroach):
 625
 absorption, lung, hamster: 675
 biosynthesis, anaerobic bacteria: 600, 601
 chlorinated derivatives, toxicity, mouse: 602
 distribution, rat: 641
 effect on
 immunity, mouse: 614
 liver microsomal drug-mobilizing enzymes,
 role of heme synthesis, rat: 646
 metabolism of other polycyclic hydrocarbons,
 rat liver: 640
 hair follicle tumors, growth rate, mouse: 920
 metabolism, rat liver microsomes, age and sex
 factors: 643
 solubilization, role of deoxyadenosine mono-
 phosphate-silver ion complex: 747
 tumor induction, planaria: 627
- BERYLLIUM
 ores, toxicity and lung tumors, animal: 678
- BETEL NUT
 chewing, oral carcinoma, Papua-New Guinea
 (coastal and highlands): 693
- BILIARY TRACT DISEASES
 cholelithiasis, gallbladder cancer, Finland:
 899
- BIPHENYL, p-AMINO-
 occupational exposure, bladder cancer: 929
- BLADDER CARCINOGENESIS
 aminobiphenyl, occupational: 929
 cyclamate, rat, review: 573
 ethylsulfonylnaphthalenesulfonamide, mouse:
 724
 historical review: 562
 industrial chemicals, human: 924
 β-naphthylamine, distant metastases, dog: 722
 non-industrial chemicals, review: 570
- BLADDER NEOPLASMS
 occupation, smoking and tryptophan metabolites,
 tumor pathology: 690
 ploidy and DNA content, invasive or non-invasive
 tumors: 922
- BLOOD GROUPS
 ABO and Rh, lung cancer, smoking, Wales: 904
- BONE MARROW
 cell cultures, effect of MC29 avian leukosis
 virus, chicken: 779
 chromosomes
 atomic radiation exposure (Hiroshima),
 healthy or leukemic persons: 591, 592
 radiation effects, rat: 590
- BONE MARROW DISEASES
 erythroid hyperplasia or myelofibrosis,
 leukemia virus particles, cat: 761
 myelofibrosis, Rauscher leukemia virus-induced,
 rat: 772
- BONE NEOPLASMS
 arrhenoblastoma, familial: 947
 chondrosarcoma
 joints, Maffucci's syndrome: 965
 possible viral etiology, human: 815

- BONE NEOPLASMS (Contd.)
 osteogenic sarcoma, radiation-induced, child: 588
 osteoma, skull, induction, hormones and/or gold thioglucose, mouse: 718
 osteosarcoma
 induction, Harvey or Moloney sarcoma virus, hamster or rat: 811
 possible viral etiology, human: 815
 Rous sarcoma virus-induced, marmoset: 798
- BRAIN
 injury by carcinogen implantation, obesity, mouse: 620
- BRAIN NEOPLASMS
 induction
 ethylnitrosourea, fetal rat: 635, 637
 methylcholanthrene, ependyoblastoma, mammary tumor virus particles, mouse: 822
 methylnitrosourea (rat): 633
 chromosomes, DNA and histones: 632
 enzymes: 631
 transplacental: 634
 Rous sarcoma virus, antibody localization, dog: 797
 trimethylbenzanthracene, chromosomes, DNA and histones, rat: 632
- BREAST NEOPLASMS (See Mammary neoplasms, human)
- BRONCHUS
 effect of cigarette or cigar smoke: 737
- BRONCHUS NEOPLASMS
 serum adenovirus-18 antibodies: 834
- BUTANE, DIEPOXY-
 effect on DNase-II, cell-free system: 612
- BUTTER YELLOW
 Hodgkin's-like lymphoma, rat: 732
- β-BUTYROLACTONE
 effect on DNase-II, cell-free system: 612
- CADMIUM
 analysis, cigarette tobacco and smoke: 686
- CARCINOGENESIS (general and unspecified)
 gene-selection theory, review: 559
 2-hit and multiple-hit theories, mathematical models: 896
- CARCINOGENESIS, CHEMICAL
 abnormal responses of non-hemocytic cells of midgut and hindgut, benzpyrene-induced, cockroach: 625
 azobenzene derivatives, structure-activity relationships, review: 571
 caustic chemicals + radiotherapy, lupus vulgaris, malignant transformation: 595
 comparison with viral carcinogenesis, review: 577
 DNA and RNA methylation, review: 567
 neoblastic tumors, planaria: 627
 polyvinylpyridine N-oxide, mouse or rat: 717
- CARCINOGENS (CHEMICAL)
 analysis, margarine or chocolate, processing methods, Germany: 604
 environmental
 lung or esophagus cancer, South Africa, ethnic groups: 928
 nasopharynx cancer, review: 568
- CARCINOGENS (CHEMICAL) (Contd.)
 permissible limits: 736
 free radical formation, organic solvents or water: 598
 non-industrial chemicals, bladder cancer, review: 570
 occupational exposure
 cancer epidemiology
 anesthesiologists, U.S. and Canada: 888
 chemists, U.S.: 933
- CELL GROWTH KINETICS
 aflatoxin- or fluorenylacetamide-induced premalignant liver nodules, rat: 671
 diethylnitrosamine-induced hepatoma, guinea pig: 654
 dimethylbenzanthracene-induced mammary tumors, hormone effects, rat: 709
- DNA contents
 mosaicism, premalignant or malignant skin tumors: 923
 non-invasive or invasive bladder cancer: 922
 preleukemic disease and leukemia, chromosomes, human: 982
 growth enhancement, substance from leukemic or normal cells, mouse embryo cells: 975
 host immunity, animal or human tumors: 945
 human leukemia: 921
 induced tumors and corresponding normal tissue, mouse or rat: 920
 invasiveness, nexus intercellular junctions, cervix cancer: 986
 Krebs cycle metabolites, growth stimulation, tumor cells *in vitro*: 615
 liver regeneration, normal or mammary tumor-bearing mouse: 941
- mathematical models
 irradiated exptl. tumor *in vivo*: 940
 lung cancer: 946
 tumor cell populations: 942
 medium pollution, cell cultures: 980
 nonviral growth-stimulating factor, Rous sarcoma virus-infected chick embryo cells: 791
 normal and malignant dividing cells, review: 587
 polyoma virus-induced tumors
 kidney sarcoma, rat: 866
 relationship to host antiviral immunity, hamster or mouse: 865
 premalignant mammary nodules, dimethylbenzanthracene-induced, hormone effects, rat: 708, 709
 psychokinetic study, exptl. mammary tumor: 985
 radiation effects *in vivo*, exptl. tumor: 940
 Rauscher virus-induced leukemia, mouse: 775
 regenerating limb, effect of liver ribonucleoprotein, frog: 984
 stomach cancer, role of intestinal metaplasia or ulceration: 939
 tissue growth-stimulating or -retarding substances, normal or malignant cells, review: 563, 564
 transplanted tumor or regenerating liver, effect of urethan, mouse: 621

CERVIX UTERI NEOPLASMS

epidemiology

- Canada (Manitoba): 894
- contraceptives, Czechoslovakia: 911
- Poland, comparison with other nations: 910
- pregnancy, Oklahoma (Oklahoma City): 906
- Pennsylvania (Philadelphia): 907
- South Africa (Cape Town), ethnic groups: 908

growth kinetics, nexus intercellular junctions and tumor invasiveness: 986

induction

- estradiol, rat: 707
- estrogen + progestagen contraceptive, mouse: 715

methylcholanthrene, rat: 707

pathogenesis: 987

possible induction by spermatic DNA: 706

pre malignant dysplasia, azathioprine-induced, human: 705

risk of second primary tumor, Connecticut: 909

serum adenovirus-18 antibodies: 834

viral etiology, review: 576

CHEEK POUCH NEOPLASMS

induction

avian adenovirus (CELO)-transformed human amnion cells, hamster: 833

dimethylbenzanthracene

effect of antilymphocyte serum, hamster: 697

estrogen or orchiectomy, hamster: 696

vitamin A, hamster: 694

succinate dehydrogenase activity, hamster: 695

CHLORAMPHENICOL

leukemia, human: 733, 734

CHOLANTHRENE

transplanted sarcoma, effect of immune serum, mouse: 623

CHROMOSOMES

abnormalities

cancer pts. and normal population: 956

Ch¹ anomaly, chronic lymphocytic leukemia, familial: 934

dimethylbenzanthracene-induced leukemia or preleukemic changes, rat: 729

leukemia risk, review: 585

occupational benzene exposure, age factors: 952

benzene-induced erythroleukemia: 951

bone marrow, atomic radiation exposure, healthy or leukemic persons, Hiroshima: 591, 592

diethylnitrosamine-induced hepatoma, guinea pig: 654

DNA content, normal or leukemic human WBC: 982

effect of nitrogen mustard derivative, Rous sarcoma virus-transformed rat cells: 796

human lymphosarcoma cell line: 978

lung tumors or smoking-induced respiratory epithelial hyperplasia: 684

malignancy-associated changes, peripheral

neutrophils, lung cancer: 949

methylnitrosourea- or trimethylbenzanthracene-induced brain tumors, rat: 632

mongolism, congenital leukemia: 953

CHROMOSOMES, (Contd.)

mosaicism, premalignant or malignant skin tumors: 923

non-invasive or invasive bladder cancer: 922

radiation effects, rat bone marrow: 590

rat embryo cells transformed by diethylnitrosamine + Rauscher leukemia virus: 776

Rous sarcoma virus-induced hamster tumor culture: 799

sex

genital, breast and other tumors, women: 955

mosaicism (XY/XO), acute myeloid leukemia: 954

testicular teratomas from male or female embryo tissue grafts, mouse: 957

COLCHICINE

mutagenesis and effect on tumor incidence, Drosophila: 626

COLLAGEN

content, spontaneously transformed mouse or rat embryo cells: 981

COLON

polyposis with soft tissue sarcomas, multiple-case family: 958

COLON NEOPLASMS

carcinoma of right colon, epidemiology, Denmark (Copenhagen): 898

from polyposis, with soft tissue sarcoma, multiple-case family: 958

malignant transformation of intestinal polyposis, phosphomonoesterase changes: 964

nuclear RNA fractionation: 950

villous adenoma, frequency of second primary tumors: 963

CONNECTIVE TISSUE

toxicity, aflatoxin or sorbic acid, rat: 699

CONNECTIVE TISSUE DISEASES (See also Immunity disorders)

Maffucci's syndrome, malignant transformation: 965

CONNECTIVE TISSUE NEOPLASMS

familial, multiple primary tumor syndrome: 914

fibrosarcoma or rhabdomyosarcoma, Rous sarcoma virus-induced, marmoset: 798

mesenchymal sarcomas of thyroid, epidemiology, Italy: 913

methylcholanthrene-induced sarcoma, transplanted, fibrinogen metabolism, mouse: 974

rhabdomyosarcoma (muscle), nickel-induced, ultrastructure, rat: 704

sarcoma, sarcoma virus particles (cell cultures) and serum antibodies, human: 815

with polyposis of colon, multiple-case family: 958

CONTRACEPTIVES

estrogen-progestagen type

cervix cancer, Czechoslovakia: 911

mouse: 715

female genital cancer, review (book): 557

osteoma of skull, mouse: 718

CORPUS UTERI NEOPLASMS

induction, alkyl nitrosoureas, pregnant, rat:

713

- CORPUS UTERI NEOPLASMS, (Contd.)
 risk of second primary tumor, Connecticut:
 909
 second primary tumor, risk, breast cancer,
 Connecticut: 909
 serum adenovirus-18 antibodies: 834
 trophoblastic, feedback hormonal mechanism and
 host immunity: 967
- CROTON OIL
 toxicity, lung, mouse: 701
- CYCASIN
 kidney tumors, Wilms' type, rat: 719
- CYCLAMATES
 bladder tumors, rat, review: 573
- CYCLOPHOSPHAMIDE (See under Antitumor agents)
- CYCLOPROPENE COMPOUNDS
 with aflatoxin, toxicity, liver, trout: 665
- DDT
 toxicity, lung, mouse: 701
- DERMATOGLYPHIC PATTERNS
 leukemia, Poland (Cracow): 916
- DIABETES MELLITUS
 cancer epidemiology, Germany (Stralsund): 891
- DIET
 high-fat/low-protein, liver cirrhosis and
 hepatoma, rat: 673
 pyridoxine-deficient, serum α_1 -fetoprotein,
 primate: 970
- DIETARY FACTORS
 esophagus and oropharynx cancer, Puerto Rico:
 932
 pyridoxine deficiency, liver cancer epidemiology,
 Africa: 970
- DIETHYLSTILBESTROL
 effect on dimethylbenzanthracene cheek pouch
 tumors, hamster: 696
- DISEASE TRANSMISSION
 cervix or prostate cancer, viral etiology,
 review: 576
 leukemia
 cluster in single house, Georgia: 917
 virus, effect of germ-free status, AKR mice:
 755
 sarcoma virus, possible, sarcoma pts. and
 their relatives: 815
- DISTRIBUTION
 aflatoxins, rat: 668, 740
 benzpyrene, rat: 641
 4'-substituted dimethylaminoazobenzenes,
 biliary metabolites, rat: 648
 transcellular glutamate migration, cell mem-
 brane properties, normal or malignant liver
 cells, rat: 976
- DUST
 occupational exposure, asbestos needles in
 lungs: 680
 silicon, occupational exposure, primary
 hemangioendothelial tumor of heart: 682
- DYES AND STAINS
 Ponceaux MX (food coloring), toxicity, liver,
 liver, mouse: 609
 printing inks, s.c. sarcoma, mouse: 607
 trypan blue or toluidine blue, mutagenesis
 and effect on tumor incidence, Drosophila:
 626
- EB VIRUS (See under Virus, herpes-type)
- ENDOCRINE ABLATION
 oophorectomy
 effect on dimethylbenzanthracene-induced
 premalignant mammary nodules, rat: 708
 mammary tumor risk, dog: 969
 orchiectomy, effect on dimethylbenzanthracene
 cheek pouch tumors, hamster: 696
- ENDOCRINE GLAND NEOPLASMS
 multiple, familial polyadenomatosis syndromes,
 review: 565
- ENVIRONMENTAL FACTORS
 cell cultures, medium pollution rates: 980
 exposure to non-industrial chemicals, bladder
 cancer, review: 570
 permissible carcinogen concentration limits:
 736
 seasonal, melanoma incidence, amphibian
 (Triturus): 628
 urbanization
 testis tumors, Denmark: 936
 tongue and lip cancer, Canada: 895
- ENZYMES
 aryl hydrocarbon hydroxylase
 and microsomal P450, effect of benzanthra-
 cene, hamster embryo cells: 647
 placenta, smoking, human: 685
- DNase
 effect of carcinogens, cell-free system:
 612
 Friend leukemia virus, mouse spleen:
 765
 glutathionase, transplanted or induced
 hepatoma, rat: 652
 histochemistry, methylnitrosourea-induced
 brain tumors, rat: 631
 metabolism, breast cancer or fibrocystic
 disease: 938
 nitrosamine breakdown in vitro, rat liver or
 kidney: 644
 phosphomonoesterase, premalignant and malignant
 intestinal polyposis: 964
 RNase, effect of Friend leukemia virus, mouse
 spleen: 765
 succinate dehydrogenase, dimethylbenzanthracene-
 induced cheek pouch tumors, hamster: 695
 thymidine kinase
 adenovirus-5 or -12-infected cells: 836
 induction, effect of temperature, SV40-
 infected cells: 874
- EPIDEMIOLOGY
 all tumors
 aged, Washington (Seattle): 893
 anesthesiologists, U.S. and Canada: 888
 associations with other diseases, aged men,
 Australia (Sydney): 892
 Canada: 894
 chemists, U.S.: 933
 children
 and adolescents, age factors, U.S.: 890
 Jamaica: 884
 diabetes mellitus, Germany (Stralsund):
 891
 East Africa: 885
 Israel: 879
 South Korea: 944

EPIDEMIOLOGY, (Contd.)

- bladder cancer, rubber and rubber antioxidant exposure, Britain: 927
- breast cancer
 - Canada: 894
 - contraceptives, review (book): 557
 - hormonal metabolism, world, review: 583
 - identification of high-risk groups, review: 582
 - risk of second primary tumor, Connecticut: 909
 - screening methods: 912
- bronchiolo-alveolar carcinoma, Finland (Helsinki): 903
- Burkitt lymphoma, Uganda (West Nile district), malaria epidemiology: 878
- cervix cancer
 - Canada (Manitoba): 894
 - contraceptives, Czechoslovakia: 911
 - Poland, comparison with other nations: 910
 - pregnancy, Oklahoma (Oklahoma City): 906
 - Pennsylvania (Philadelphia): 907
 - viral etiology, review: 576
 - South Africa (Cape Town), ethnic groups: 908
- chromosome abnormalities, cancer pts. and normal population: 956
- colon cancer, Denmark (Copenhagen): 898
- esophagus cancer
 - environmental carcinogens, South Africa, ethnic groups: 928
 - smoking and dietary factors, Puerto Rico: 932
- female genital tumors
 - contraceptives, review (book): 557
 - risk of second primary tumors, Connecticut: 909
- gallbladder cancer, Finland, cholelithiasis: 899
- kidney tumors, review: 581
- larynx cancer, smoking and occupation, Czechoslovakia: 881
- leukemia
 - cluster (multiple-case house), Georgia: 917
 - dermatoglyphic abnormalities, Poland (Cracow): 916
 - genetic factors: 918
 - high-risk groups, chromosomal defects, review: 585
 - radiotherapy-induced, Japan, review: 561
 - review: 586
 - viral etiology, review: 578
- life expectancy, smoking, U.S. men: 900
- liver cancer, dietary pyridoxine deficiency, Africa: 970
- lung cancer
 - air pollution, proposed community health studies: 902
 - review: 574
 - Canada: 894
 - environmental carcinogens, South Africa, ethnic groups: 928
 - smoking, review: 569, 574
 - South Africa, ethnic groups, smoking: 901, 928
 - Wales (Swansea), ABO and Rh blood groups, smoking: 904

EPIDEMIOLOGY, (Contd.)

- lymphoma, associated high-risk disorders (immunity disorders), review: 585
- melanoma, sun exposure, Australia, review: 558
- mesenchymal tumors of thyroid, Italy: 913
- mouth cancer
 - Canada, comparison with other nations: 895
 - India (rural), tobacco use: 935
 - Papua-New Guinea (coastal and highlands), betel chewing: 693
 - Puerto Rico, smoking and dietary factors: 932
- multiple primary tumors of upper g.i. or respiratory tract, smoking: 931
- myeloma, Japan, myeloma globulin types, comparison with New York (white and Negro) group: 915
- nasopharynx cancer
 - genetic and environmental factors, review: 568
 - possible genetic susceptibility to tumor virus, Hong Kong, ethnic groups: 825
- pharynx cancer, smoking and dietary factors, Puerto Rico: 932
- prostate cancer, viral etiology, review: 576
- respiratory cancer
 - Italy (Genoa): 905
 - occupational arsenic exposure, U.S.: 926
- second primary tumors associated with chronic lymphatic leukemia: 882
- serum adenovirus antibodies
 - human cancer: 834
 - nasopharynx cancer, Hong Kong: 825
- serum EB virus antibodies
 - nasopharynx cancer, Asia (Japanese or Chinese): 825, 925
- skin cancer, occupational, Britain: 889
- stomach cancer
 - Poland: 897
 - two-hit and multiple-hit theories of carcinogenesis, mathematical models: 896
- testis tumors, Denmark, urban and rural: 936
- thyroid cancer
 - Israel: 883
 - Minnesota (Olmsted County; Rochester): 887
 - radiation exposure, Japan (Hiroshima/Nagasaki): 930
 - review: 584
- EPIDEMIOLOGY, VETERINARY
 - leukemia, role of hairless (hr) gene, mouse: 919
 - mammary and lung tumors, spontaneous, mouse strains: 983
- EPSTEIN-BARR VIRUS (See under Virus, herpes-type)
- ESOPHAGUS NEOPLASMS
 - epidemiology
 - environmental carcinogens, South Africa, ethnic groups: 928
 - smoking and dietary factors, Puerto Rico: 932
 - following radiation cure of tracheal cancer: 593
- malignant transformation of marginal diverticulum: 1000
- of megaesophagus: 961

- ESTRADIOL
osteoma of skull, mouse: 718
- ESTRADIOL BENZOATE
cervix or skin tumors, rat: 707
- ESTRONE
pituitary tumors, plasma prolactin levels,
male rat: 728
- ETHER, BIS(CHLOROMETHYL)-
lung tumors, mouse: 676
- ETHER, CHLOROMETHYL METHYL-
lung tumors, mouse: 676
- ETHNIC GROUPS
cervix cancer, South Africa (Cape Town): 908
esophagus cancer, environmental carcinogens,
South Africa: 928
lung cancer, smoking and other carcinogen
exposure, South Africa: 901, 928
mouth cancer, France and Canada (Quebec): 895
nasopharynx cancer, Hong Kong: 825
- EYE NEOPLASMS
melanoma, induction, urethan or hydroxyurethan,
rat: 629
- FATS
dietary excess, liver cirrhosis and hepatoma,
rat: 673
margarine or chocolate, carcinogen content,
processing methods, Germany: 604
- FIBRINOGEN
metabolism, transplanted mouse tumors: 974
- 2-FLUORENAMINE
toxicity, insect (cockroach): 624
- N-2-FLUORENYLACETAMIDE
premalignant liver nodules, in vitro growth
rate, rat: 671
- N-2-FLUORENYLACETAMIDE, N-HYDROXY-
metabolism, effect of sulfate ion, rat liver:
672
- FOOD ADDITIVES
food coloring (Ponceau MX), liver toxicity,
mouse: 609
hexamethylenetetramine, toxicity, mouse or rat:
608
- FOODS
animal feeds, aflatoxin contents and toxicity,
review: 572
cyclamates or cyclamate-saccharin mixture,
bladder tumors, rat, review: 573
margarine or chocolate, carcinogen content,
processing methods, Germany: 604
nitrates, reduction to nitrosamine (gastric
bacteria), human: 639
refrigeration, aflatoxin production: 661
wheat flour, nitrosamine content, analytical
method: 610
- FUNGI
steroid-hydroxylating strains, aflatoxin
metabolism: 662
- GALLBLADDER NEOPLASMS
epidemiology, Finland, cholelithiasis: 899
- GASTROINTESTINAL CARCINOGENESIS
nitroquinoline oxide, intestine, rat: 674
nitrosamines, DNase and RNase, high- and low-
tumor sites, rat: 971
- GASTROINTESTINAL CARCINOGENESIS, (Contd.)
N-nitroso compounds, upper g.i. tract, tumor
pathology, rat: 638
possible mechanism (nitrate reduction to
nitrosamine), human: 639
- GASTROINTESTINAL NEOPLASMS
epidemiology, anesthesiologists, U.S. and
Canada: 888
- GENETICS, ANIMAL
leukemia, role of hairless (hr) gene, mouse:
919
possible latent virus and host immunity, high-
plasma cell tumor mouse strain: 973
serum complement activity, NZB mice and
hybrids: 972
strain differences
FBJ sarcoma virus sensitivity, mouse: 814
nickel-induced rhabdomyosarcoma, rat: 704
Rauscher virus-induced lymphoma, mouse:
774
spontaneous mammary and lung tumors, mouse:
983
strain-specific immunity disorders, leukemia
virus-like particles, NZB mice: 871
- GENETICS, CELLULAR
gene-selection theory of carcinogenesis,
review: 559
SV40- or polyoma-transformed cells, review:
580
- GENETICS, HUMAN
familial
arrhenoblastoma: 947
chromosome abnormalities, cancer pts. and
normal subjects: 956
Ch¹ anomaly, chronic lymphatic leukemia:
934
immunity disorders with chronic leukemia:
959
leukemia: 918, 943
pheochromocytoma (epinephrine-producing)
with medullary carcinoma of thyroid:
948
polyadenomatosis syndromes, review: 565
polyposis (Peutz-Jeghers), stomach cancer,
child: 962
soft-tissue sarcomas with breast and other
tumors: 914
with colon polyposis: 958
tumors of ovary, mother and daughters: 886
high-risk disorders, leukemia and lymphoma,
review: 585
leukemia epidemiology, review: 586
mongolism, with congenital leukemia: 953
- GENETICS, MICROBIAL
adenovirus-2 genome transcription, infected
or transformed cells: 835
- GENETICS, POPULATION
myeloma globulin distribution, Japan and New
York (white and Negro): 915
nasopharynx cancer, Hong Kong, ethnic groups:
825
Orientals and other populations, review:
568
- GENITAL NEOPLASMS, FEMALE
epidemiology, contraceptives, review (book):
557
induction, ethylnitrosourea, pregnant rat: 721

INITIAL NEOPLASMS, FEMALE, (Contd.)

multicentric tumors of cloacal origin,
pathogenesis: 960
risk of second primary tumor, Connecticut:
909
sex chromatin, human: 955

RM-FREE STATUS

effect on

dimethylbenzanthracene carcinogenesis,
mouse: 611, 702, 703, 731
leukemia virus transmission, AKR mice: 755
mouse, review: 575
mammary tumor virus infection and trans-
mission, mouse, review: 575
methylcholanthrene s.c. tumors, mouse: 611
radiation leukemogenesis, mouse: 589
Rous sarcoma virus oncogenesis, rat: 790

YCOPROTEINS

distribution, polyoma virus-induced hamster
sarcoma: 862

D THIOGLUCOSE

osteoma of skull, mouse: 718

RT NEOPLASMS

hemangioendothelial, occupational silicosis:
682

AMETHYLENETETRAMINE (food additive)

toxicity, mouse and rat: 608

TONES

content, methylnitrosourea- or trimethyl-
benzanthracene-induced brain tumors, rat:
632

MONES

estradiol or deoxycorticosterone, mammary
nodule induction, effect of thymectomy,
mammary tumor virus-infected mouse:
820, 821

estrogen, enhancement of dimethylbenzene cheek
pouch carcinogenesis, intact or orchiecto-
mized hamster: 696

estrogen-progestagen contraceptives

cervix cancer, Czechoslovakia: 911
mouse: 715

growth-stimulating or -retarding, production
and effects on normal and malignant cells,
review: 563, 564

metabolic patterns, breast cancer epidemiology,
world, review: 583

pituitary graft, effect on hyperplastic

alveolar mammary nodule, mouse: 710, 819

placental steroids and chorionic gonadotropin,
feedback mechanism, normal pregnancy and
trophoblastic tumors: 967

rolactin

metabolism, estrone-induced or spontaneous
pituitary tumors, rat: 728

spontaneous mammary tumors, rat: 728

radioimmunoassay, normal pituitary or
prolactin-producing pituitary tumor,
rat: 727

OCARBONS, POLYCYCLIC AROMATIC

air pollution, detection method: 603

metabolism, effect of benzpyrene, rat liver:
640

structure-activity relationships, nuclear

magnetic resonance spectra: 599

IMMUNITY

cellular

antibodies to HeLa cell antigen, human
tumors: 751

antigen specific for tumor mitochondria,
transplanted or virus-induced animal
tumors: 788

Epstein-Barr virus, human cells: 828, 829

Graffi or Moloney leukemia/sarcoma virus-
infected cells: 762

herpes simplex virus-infected hamster cells:
824

membrane and viral antibodies, Burkitt
lymphoma cells: 827

polyoma virus-transformed cells, review:
580

SV40

induced hamster tumors: 850

transformed cells: 848

review: 580

T antigen, SV40-infected cells: 849,
851, 874

tumor-specific antigens, diethylnitrosamine

hepatoma, guinea pig: 655, 656

methylcholanthrene sarcoma, guinea pig
or mouse: 657, 658

U antigen, temperature effects, SV40-
infected cells: 874

Freund's adjuvant, effect on urethan-induced
lung tumors, mouse: 677

host

adenovirus antibodies, nasopharynx and
other human cancer: 825, 834

EB virus antibodies, nasopharynx cancer or
Burkitt lymphoma: 825, 826

effect of carcinogens, mouse: 614

FBJ osteosarcoma virus-infected mouse: 814

Friend virus-induced rat tumor: 764

Gross leukemia virus-induced mouse lymphoma:
763

high-plasma cell tumor mouse strain, age
changes: 973

Moloney leukemia virus

induced lymphoma, mouse: 770

infected rat: 768

Moloney sarcoma virus-induced tumors,

effect of antitumor agent and/or immune
serum, mouse: 808

normal pregnancy and trophoblastic tumors,
human: 967

polyoma virus

induced animal tumors: 865

induction, antilymphocyte serum, mouse:
864

radiation effects, mouse or hamster:
855, 856

radiation effects, mathematical model,
mouse tumor: 940

Rauscher leukemia virus-induced tumor
immunity, mouse: 773

relationship to tumor growth and rejection,
review: 566

Rous sarcoma virus-induced tumor, dog: 797
hamster: 800

sarcoma virus, sarcoma pts. and their
relatives: 815

SV40-induced hamster tumors: 850

IMMUNITY, (Contd.)

tumor growth rate, animal or human: 945
tumor-specific transplantation immunity,
induction, animal: 789, 845

viral

avian myeloblastosis virus-rabbit antibody
complex, properties: 778
Graffi or Moloney leukemia/sarcoma virus-
infected cells: 762
group-specific antigen, adenovirus-12,
isolation and properties: 838
avian leukosis-sarcoma virus complex,
properties: 777

IMMUNITY DISORDERS (See also Connective tissue diseases)

immunoglobulin deficiency with leukemia,
familial: 959
leprosy, cancer risk, U.S.: 880
lupus vulgaris, malignant transformation: 595
lymphoma risk, review: 585
strain-specific, leukemia-like virus, NZB
mice: 871

IMMUNOSUPPRESSION

antilymphocyte serum
effect on
dimethylbenzanthracene tumors, germ-free
mouse: 703
hamster cheek pouch: 697
herpesvirus infection, mouse: 875
transplantable tumors, mouse: 623
host immunity induction, polyoma virus-
infected mouse: 864
azathioprine, induction of cervical dysplasia,
human: 705
cyclophosphamide, effect of immune sera,
Moloney virus-induced sarcoma, mouse: 808
dimethylbenzanthracene, newborn or adult mouse:
614
Friend leukemia virus, mouse: 766
SV40, hamster: 767

INJURIES (See also under Scar tissue)

brain, implanted carcinogen, obesity induction,
mouse: 620

premalignant tumors of lip: 594

INKS (See under Dyes and stains)

INSECTICIDES

DDT, toxicity, lung, mouse: 701

INSECTS

cockroach

benzpyrene-induced abnormal cellular
responses (non-hemocytic cells of midgut
and hindgut): 625
carcinogen toxicity: 624

Drosophila, high- or low-tumor strains, effect
of phthalate compounds and other agents:
626

INTERFERON

attempted induction, mammary tumor virus,
mouse: 823
inducer, effect on mouse sarcoma or leukemia
viruses in vitro: 843
loss of responsiveness, mechanism, Moloney
sarcoma virus-infected mouse embryo cells:
805

INTESTINE, LARGE, NEOPLASMS

second primary tumor, risk, breast or
female genital cancer, Connecticut: 909

IODODEOXYURIDINE (See under Antitumor agents)

JOINT NEOPLASMS

chondrosarcoma, Maffucci's syndrome: 965

KIDNEY

calf, cell line (CK-66), virus-like particles:
752

nitrosamine breakdown in vitro, rat: 644
toxicity, lead acetate, hamster: 720

KIDNEY CARCINOGENESIS

cycasin, Wilms' tumors, rat: 719
dimethylnitrosamine, rat: 721
tumor transplantability, rat: 725
lead acetate, mouse: 720
transplacental, mouse: 714

KIDNEY NEOPLASMS

epidemiology, review: 581
nuclear DNA fractionation: 950
polyoma virus-induced sarcoma, growth patterns,
rat: 866

LARYNX NEOPLASMS

epidemiology, smoking and occupation,
Czechoslovakia: 881

LEAD

analysis, cigarette tobacco and smoke: 686

LEAD ACETATE

kidney tumors (mouse) and toxicity (hamster):
720

LEPROSY

cancer epidemiology, U.S.: 880

LEUKEMIA, EXPERIMENTAL (See also under Virus, leukemia/lymphoma)

CFW_w cell-transmitted (mouse), leukemia
virus particles: 756
erythroleukemia or erythremic myelosis, feline
leukemia virus particles, cat: 761
genetic susceptibility, role of hairless (hr)
locus, mouse: 919
myeloid, with myelofibrosis, Rauscher leukemia
virus-induced, rat: 772
P-1081 radiation-induced, growth-enhancing
substance, mouse embryo cells: 975
Rauscher leukemia virus-induced, pathology,
mouse: 771, 775
rat: 771
viral etiology, review: 578

LEUKEMIA, HUMAN

acute myeloblastic, XY/XO mosaicism with group
G deletion: 954
atomic radiation exposure (Hiroshima), bone
marrow chromosomes: 592
cell growth kinetics: 921
cell lines, surface antigens to EB virus: 829
chromosomal DNA content: 982
chronic lymphocytic
associated immunity disorders, familial:
959
Ch¹ chromosomal anomaly, familial: 934
incidence of second primary tumor: 882
congenital, mongolism: 953
epidemiology
anesthesiologists, U.S. and Canada: 888

LEUKEMIA, HUMAN, (Contd.)

dermatoglyphic abnormalities, Poland (Cracow): 916
genetic factors: 918
high-risk associated disorders (chromosomal defects), review: 585
leprosy, U.S.: 880
radiotherapy-induced leukemia, Japan, review: 561
review: 586
viral etiology, review: 578
familial: 943
lymphocyte blastoid transformation, review: 560

multiple-case house, Georgia: 917

LEUKEMOGENESIS, EXPERIMENTAL

chick erythroblastosis virus, rat: 754
dimethylbenzanthracene
germ-free mouse: 731
preleukemic stage, bone marrow chromosomes, rat: 729
polyvinylpyridine N-oxide, mouse or rat: 717
Rauscher mouse leukemia virus, leukemia or lymphoma with myelofibrosis, rat: 772

LEUKEMOGENESIS, HUMAN

benzene, occupational, chromosomes: 951, 952
chloramphenicol: 733, 734

LEU NEOPLASMS

epidemiology, Canada, urban and rural: 895
preinfectious, role of herpes infection or injury: 594

LEPID

metabolism, breast cancer or fibrocystic disease: 938

LEVER

glycogen, organ-specific effect of thioacetamide, mouse: 660
hydroxyfluorenylacetamide metabolism, effect of sulfate ion, rat: 672
lysosomes, effect of aflatoxin, rat: 670
microsomal metabolism, effect of carcinogens, rat: 642, 643, 645, 646
nitrosamine breakdown *in vitro*, rat: 644
polycyclic aromatic hydrocarbon metabolism, effect of benzpyrene, rat: 640
regeneration, normal or mammary tumor-bearing mouse: 941
soluble proteins during carcinogenesis, rat: 651
toxicity
aflatoxins, fish: 665, 666
food coloring (Ponceau MX), mouse: 609

LEVER CARCINOGENESIS

aflatoxin
+ cyclopropenes, trout: 665
preinfectious, growth rate *in vitro*, rat: 671
species difference, salmon or trout: 666
diethylnitrosamine
synergism with Mott hepatitis virus, mouse: 653
tumor pathology, chromosomes and growth rate, guinea pig: 654
tumor-specific antigens, guinea pig: 655, 656
dimethylaminoazobenzene
effect of dimethylbenzanthracene, rat: 650

LIVER CARCINOGENESIS, (Contd.)

host factors, rat: 659
tumor growth rate, rat: 920
dimethylbenzanthracene, germ-free mouse: 611, 702
dimethylnitrosamine, rat: 721
fluorenylacetamide, premalignant, growth rate *in vitro*, rat: 671
high-fat/low-protein diet inducing cirrhosis, rat: 673
methylmethylaminoazobenzene
glutathione activation, rat: 652
soluble liver proteins, rat: 651

LIVER NEOPLASMS

epidemiology, dietary pyridoxine deficiency, Africa: 770
rat hepatoma, cells, effect of dimethylaminoazobenzene: 613
transplanted or induced, glutathione, rat: 652

LUNG

asbestos bodies
occupational asbestos or dust exposure: 680
structure and development, hamster: 679
dimethylbenzanthracene or benzpyrene absorption, hamster: 675

LUNG CARCINOGENESIS

antitumor agent (ibenzmethylin), mouse: 605
beryllium, rat: 678
bis(chloromethyl)ether, mouse: 676
chloromethyl methyl ether, mouse: 676
dimethylbenzanthracene, germ-free or "minimal-disease" mice: 702, 703
nitroquinoline oxide, rat: 674
screening method, newborn mouse: 701
transplacental, mouse: 714
urethane, effect of Freund's adjuvant, mouse: 677

LUNG NEOPLASMS

adenoma or bronchogenic carcinoma, chromosomes: 684
bronchiolo-alveolar carcinoma, epidemiology, Finland (Helsinki): 903
epidemiology
air pollution, review: 574
anesthesiologists, U.S. and Canada: 888
Canada: 894
environmental carcinogens, South Africa, ethnic groups: 928
smoking, review: 569, 574
South Africa, ethnic groups: 901, 928
strain differences, mouse: 983
growth rate, mathematical model: 946
malignancy-associated chromatin changes, peripheral neutrophils: 949

LYMPHOMA, MALIGNANT, EXPERIMENTAL

FVTCT reticulum cell sarcoma (mouse), recovery of Friend leukemia virus: 769
Gross leukemia virus-induced, host immunity, mouse: 763
incidence, Wistar rats: 732
induction, rat-adapted erythroblastosis virus, extrathymic lymphomas, rat: 753
2731/L (mouse), from reovirus-infected mouse, association with Gross-AKR type leukemia virus: 757

LYMPHOMA, MALIGNANT, EXPERIMENTAL, (Contd.)

- lymphosarcoma, with myelofibrosis, Rauscher leukemia virus-induced, rat: 772
- Moloney leukemia virus-induced, splenic antibodies, mouse: 770
- radiation induction, germ-free or conventional mice: 589
- Rauscher leukemia virus-induced
 - pathology, mouse: 771
 - strain difference, mouse: 774

LYMPHOMA, MALIGNANT, HUMAN

- Burkitt's
 - EB virus
 - detection method: 828
 - differentiation of membrane and viral immunofluorescence antibodies: 827
 - positive cell lines, properties: 829, 831
 - properties: 830
 - serum antibodies: 826
 - possible association with endemic malaria, Uganda (West Nile district): 878
- epidemiology
 - anesthesiologists, U.S. and Canada: 888
 - chemists, U.S.: 933
 - high-risk associated disorders (immunity deficiencies), review: 585
 - leprosy, U.S.: 880
- lymphosarcoma, cell line, ultrastructure: 978

MALARIA

- possible association with Burkitt lymphoma, Uganda (West Nile district): 878

MALIGNANT TRANSFORMATION

- benign nevus to melanoma, mechanism, review: 558
- cholelithiasis to gallbladder cancer, Finland: 899
- familial polyposis (Peutz-Jeghers) to stomach cancer, child: 962
- idiopathic megaesophagus to cancer of esophagus: 961
- injury or herpes infection to premalignant or malignant lip neoplasms: 594
- intestinal polyposis to colon cancer, phosphomonoesterase: 964
- lupus vulgaris to skin cancer, sun exposure or radiotherapy: 595
- lymphocyte blastoid transformation, significance, review: 560
- peptic ulcer to stomach cancer: 596, 939
- rodent ulcer to basal cell carcinoma (ulcus terebrans type), pathology: 988
- spontaneous, mouse, rat or hamster embryo cell cultures: 977, 979, 981

MAMMARY CARCINOGENESIS, EXPERIMENTAL

- alkylnitrosoureas, pregnant rat: 713
- dimethylbenzanthracene (rat): 711
 - cytochemistry: 649, 938
 - premalignant nodules, growth rate and hormone effects: 708, 709
 - tumor growth rate: 709, 920
- ethylsulfonylnaphthalene-1-sulfonamide, mouse: 724
- polyvinylpyridine N-oxide, mouse or rat: 717

MAMMARY CARCINOGENESIS, EXPERIMENTAL, (Contd.)

- mammary tumor virus + hormones, effect of thymectomy, mouse: 820, 821
- urethan and derivative (butyl carbamate), mouse: 712

MAMMARY NEOPLASMS, EXPERIMENTAL (See also Virus, mammary tumor)

- epidemiology, genetics, mouse strains: 983
- hyperplastic alveolar nodules
 - effect of mammary tumor or nodule-inducing virus, mouse: 819
 - methylcholanthrene, mouse: 819
 - hormone effects, mouse: 710, 819
- liver regeneration pattern, mouse: 941
- mammary tumor virus replication and ultrastructure, mouse: 816, 817
- risk, effect of spaying, dog: 969
- spontaneous, plasma prolactin, rat: 728
- transplantable
 - effect of immune sera, mouse: 623
 - fibrinogen metabolism, mouse: 974
 - psychokinetic effects, mouse: 985

MAMMARY NEOPLASMS, HUMAN

- benign fibroadenoma, malignant transformation (cystosarcoma phyllodes): 996
- epidemiology
 - Canada: 894
 - chemists, U.S.: 933
 - contraceptives, review (book): 557
 - hormonal metabolism, world, review: 583
 - identification of high-risk groups, review: 582
 - screening methods: 912
 - frequency of pituitary metastases: 966
 - lipid, enzyme and nucleic acid histochemistry: 938
 - risk of second primary tumor, Connecticut: 909
 - serum adenovirus-18 antibodies: 834
 - sex chromatin: 955

MESIDINE

- toxicity, lung, mouse: 701

METABOLISM (glycolysis and respiration)

- dimethylbenzanthracene-induced ovary or mammary tumors, mouse: 649
- Krebs cycle metabolites, stimulation of tumor cells *in vitro*: 615

METALS, HEAVY

- analysis, cigarette tobacco and smoke (filtered or unfiltered): 686

3-METHYLCHOLANTHRENE

- absence of s.c. tumors, squirrel monkey: 700
- brain tumor (ependymoblastoma), mammary tumor virus particles, mouse: 822
- cervix or skin tumors, rat: 707
- effect on
 - immunity, mouse: 614
 - liver microsomes, rat: 645
 - tumor development, transplanted hyperplastic alveolar mammary nodule, mouse: 819
- muscle sarcoma, transplanted, fibrinogen metabolism, mouse: 974
- neoblastic tumors, planaria: 627
- s.c. sarcoma
 - germ-free mice: 611
 - tumor-specific antigens, mouse or guinea pig: 657, 658

METHYLCHOLANTHRENE, (Contd.)

- skin tumors, effect of dimethylaminostilbene, rat: 659
- with testosterone, prostate tumors, histochemistry, mouse: 716
- toxicity, insect (cockroach): 624
- transplantable sarcoma, effect of heparin, epsilon-aminocaproic acid or splenectomy, mouse: 622

TOMYCIN C (See under Antitumor agents)

TOSIS

- synchronization, mathematical model, tumor cells: 942

UTHEROPLASMS

epidemiology

- Canada, comparison with other nations: 895
- India (rural), smoking and tobacco chewing: 935
- Papua-New Guinea (coastal and highlands), verrucous carcinoma, betel chewing: 693
- Puerto Rico, smoking and dietary factors: 932
- multiple primary type, epidemiology, smoking: 931

COPOLYSACCHARIDES

- distribution, polyoma virus-induced hamster sarcoma: 862

GENESIS

- 1-nitroso-2-imidazolidone, Saccharomyces: 742
- nitrosourea compounds, structure-activity relationship: 741

- phthalate compounds and other agents, Drosophila: 626

LOFIBROSIS (See under Bone marrow diseases)

LOMA AND RELATED DISEASES

- epidemiology, Japan, myeloma globulin types, comparison with New York (white and Negro) group: 915
- mineral oil-induced plasmacytoma, mammary tumor virus-like particles, mouse: 730
- plasma cell tumors, host immunity and possible latent leukemia virus, mouse strain: 973

HTHALENE-1-SULFONAMIDE, 4-ETHYLSULFONYL-mammary and bladder tumors, mouse: 724

HTHOL AND NAPHTHALENE DERIVATIVES

- carcinogenic or noncarcinogenic, free radical formation, organic solvents or water: 598

APHTHYLAMINE

- bladder tumors, distant metastases, dog: 722

OPHARYNX NEOPLASMS

epidemiology

- genetic and environmental factors, review: 568
- possible virus susceptibility, Hong Kong, ethnic groups: 825
- serum EB virus antibodies: 826, 925

PLASMS, EXPERIMENTAL

- AH-130 hepatoma (rat), tumor mitochondria-specific antigen: 788

- formation of metastases, role of RES, mouse: 622

- friend virus-infected cell lines, host immunity, rat: 764

- germ-free rats, carcinogen- or radiation-induced, absence of tumor viruses, review: 575

NEOPLASMS, EXPERIMENTAL, (Contd.)

- growth rate, host immunity: 945
 - immunity, review: 566
 - incidence, effect of phthalate compounds and other agents, Drosophila: 626
 - Kirsten (mouse) sarcoma virus-induced hamster sarcoma, hamster-specific sarcoma virus: 801
 - MFS8 fibrosarcoma (mouse), cells, stimulation by Krebs cycle metabolites: 615
 - Moloney (Gross pseudotype) sarcoma virus-induced hamster tumor, hamster-specific sarcoma virus: 802
 - MSB-1 tumor (rat), Moloney sarcoma virus rescue, Moloney leukemia virus-infected mouse: 804
 - polyoma virus-induced (hamster) radiation effects: 855, 856
 - sarcoma, glycoprotein distribution: 862
 - RAB-1 sarcoma (mouse), Graffi leukemia virus isolation: 813
 - radiation effects in vivo, mathematical model: 940
 - rat hepatoma, cell membrane transport: 976
 - Rous sarcoma virus-induced (hamster) reovirus particles: 758
 - sarcoma, properties of long-term cell line: 799
 - spontaneously transformed embryo cells mouse, rat or hamster, properties: 977, 979
 - virus particles and collagen content, mouse or rat: 981
 - synchronized mitosis, mathematical model: 942
 - tumor mitochondria-specific antigen, virus-induced or transplanted tumors, mouse, rat or hamster: 788
 - transplantable effect of urethan or DNA or RNA, mouse: 621
 - sarcoma, effect of immune serum, mouse: 623
- NEOPLASMS, HUMAN (general and unspecified)
- carcinoma or sarcoma, serum adenovirus-18 antibodies: 834
 - cellular antibodies to HeLa cell antigen: 751
 - detection of Epstein-Barr virus particles, method: 828
 - epidemiology adolescents and children, age factors, U.S.: 890
 - aged, Washington (Seattle): 893
 - associations with other diseases, aged men, Australia: 892
 - Canada: 894
 - children, Jamaica: 884
 - diabetes mellitus, Germany (Stralsund): 891
 - East Africa: 885
 - Israel: 879
 - leprosy, U.S.: 880
 - South Korea: 944
 - frequency of constitutional and/or familial chromosome abnormalities: 956
 - pituitary metastases: 966
 - growth rate, host immunity: 945
 - immunity, review: 566
 - lymphocyte blastoid transformation, review: 560

NEOPLASMS, HUMAN, (Contd.)

- multiple primary
 - soft tissue sarcoma, breast cancer and other tumors, familial: 914
 - trachea (radiation-cured), esophagus and prostate: 593
 - second primary tumors
 - incidence, chronic lymphocytic leukemia: 882
 - risk, breast or female genital cancer, Connecticut: 909
 - virus superinfection: 869
- NERVOUS SYSTEM NEOPLASMS (See also Brain neoplasms)
- induction
 - ethylnitrosourea, fetal rat: 635, 637
 - methylnitrosourea, newborn or fetal rat: 634
 - rat: 633
 - phenyldimethyltriazine, rat: 636

NICKEL

- analysis, cigarette tobacco and smoke: 686
- rhabdomyosarcoma of muscle, strain difference, rat: 704
- ultrastructure, rat: 704

NITRATES

- reduction to nitrosamine (gastric bacteria), human: 639

NITROGEN MUSTARD (See under Antitumor agents)

4-NITROQUINOLINE 1-OXIDE

- effect on deoxyribonucleosides, nuclear magnetic resonance spectra: 597
- intracerebral implant, induction of obesity, mouse: 620
- nitro reduction, rat liver microsomes: 642
- reaction with phenols: 745
- s.c. sarcoma, lung and intestinal tumors, rat: 674
- synthesis: 744
- tritiated, synthesis: 743

NITROSAMINES

- enzymatic breakdown, rat liver or kidney: 644
- g.i. tumors, DNase and RNase, high- and low-tumor sites, rat: 971
- production, gastric bacteria, human: 639

NITROSAMINE, DIETHYL-

- analysis, method, wheat flour: 610
- combined with Rauscher mouse leukemia virus, transformation, rat embryo cells: 776
- hepatoma
 - pathology, chromosomes and growth rate, guinea pig: 654
 - synergism with possible hepatitis virus, mouse: 653
 - tumor-specific antigens, guinea pig: 655, 656
- lung tumors, mouse: 701

NITROSAMINE, DIMETHYL-

- kidney tumors
 - fetal mouse: 714
 - rat: 721
 - transplantability, rat: 725
- liver tumors, rat: 721
- lung tumors, fetal mouse: 714

NITROSO COMPOUNDS

- synthesis from carcinogenic arylhydroxylamines: 738

NITROSO COMPOUNDS, (Contd.)

- upper g.i. tumors, pathology, rat: 638
- 1-NITROS0-2-IMIDAZOLIDONE
- mutagenesis, *Saccharomyces*: 742
- NITROSUREA COMPOUNDS
- mutagenesis, structure-activity relationship: 741
- N-NITROSUREA, N-ETHYL-
- brain and peripheral or cranial nerve tumors, fetal rat: 635, 637
 - mammary and female genital tumors, pregnant rat: 713, 723
- N-NITROSUREA, N-METHYL-
- brain tumors
 - DNA and chromosomes, rat: 632
 - fetal or newborn rat: 634
 - histochemistry, rat: 631, 632
 - rat: 633
 - cranial or peripheral nerve tumors
 - fetal or newborn rat: 634
 - rat: 633
 - lung or kidney tumors, fetal mouse: 714
 - mammary or genital tumors, pregnant rat: 713
 - spinal cord tumors, fetal or newborn rat: 634
- NUCLEASES
- acid and alkaline DNase and RNase, high- and low-carcinoma sites, rat g.i. tract: 971
- DNase
- effect of carcinogens, cell-free system: 612
 - spleen, effect of Friend leukemia virus, mouse: 765
- RNase, spleen, effect of Friend leukemia virus, mouse: 765
- NUCLEIC ACIDS, DNA
- adenovirus-infected or -transformed cells: 835, 836, 837, 838
 - avian myeloblastosis virus-infected cells: 780
 - effect of
 - bromomethylated benzantracenes or anthracenes, normal cells: 619
 - carcinogens, cell-free system: 667
 - hydroxyaminoquinoline, bacteria: 616
 - methylnitrosourea *in vivo*, rat: 630
 - urethan, transplanted tumor or regenerating liver, mouse: 621
 - Epstein-Barr virus, properties: 831
 - euchromatin or heterochromatin, normal or leukemic human WBC: 882
 - mammalian, toxicity, amphibian: 628
 - metabolism, breast cancer or fibrocystic disease: 938
 - methylation, review: 567
 - methylnitrosourea- or trimethylbenzantracene-induced brain tumors, rat: 632
 - Moloney leukemia virus-infected cells: 806
 - Moloney sarcoma virus-infected or -transformed cells: 803, 806
 - poiroma virus, non-infectious supercoiled type: 861
 - pre malignant or malignant bladder or skin tumors, human: 922, 923
 - Rous sarcoma virus-infected or -transformed cells: 780, 795
 - spermatic, possible induction of cervix cancer: 706

- CLEIC ACIDS, DNA, (Contd.)
 SV40, transformation and T antigen induction, diploid human cells: 851
 viral carcinogenesis, mechanism, review: 577
 CLEIC ACIDS, RNA
 adenovirus-infected or -transformed cells: 835, 839
 bacteriophage, effect on adenovirus-12 tumor induction, hamster: 840
 effect of urethan, transplanted tumor or regenerating liver, mouse: 621
 mammalian, toxicity, amphibian: 628
 metabolism, breast cancer or fibrocystic disease: 938
 methylation, review: 567
 Moloney leukemia virus-infected cells: 806
 Moloney sarcoma virus-infected or -transformed cells: 803, 806
 nuclear, fractionation, normal or malignant human cells: 950
 Rous sarcoma virus
 infected cells with/without nuclear fragmentation: 795
 possible subunit structure: 784
 viral carcinogenesis, mechanism, review: 577
 CLEIC ACIDS, RNA, SYNTHETIC POLYMER (polyinosinic:polycytidylic acid)
 effect on
 adenovirus-12 tumor induction, hamster: 840
 Friend virus leukemogenesis, mouse: 841
 mouse sarcoma or leukemia viruses in vitro: 843
 SV40 tumor induction, hamster: 842
 LEOPROTEINS
 ribonucleoprotein, effect on limb regeneration, frog: 984
 RNA, Rous sarcoma virus A and C particles, transformed cells: 787
 EOSIDES AND NUCLEOTIDES
 deoxythymidine and other deoxyribonucleosides, effect of nitroquinoline oxide, nuclear magnetic resonance spectra: 597
 OCCUPATIONAL DISEASES
 aminobiphenyl exposure, bladder cancer: 929
 arsenic exposure, respiratory cancer, U.S.: 926
 asbestos exposure
 asbestos needles in lungs: 680
 pleural and peritoneal mesothelioma: 681
 flatoxin exposure, possible toxic dermatosis: 669
 benzene exposure
 chromosomal abnormalities, age factors: 952
 erythroleukemia, chromosomes: 951
 adder cancer: 690, 920
 cancer incidence, anesthesiologists, U.S. and Canada: 888
 environmental carcinogen exposure
 larynx cancer, Czechoslovakia: 881
 lung or esophagus cancer, South Africa, ethnic groups: 928
 polymerized rubber additive exposure, cancer risk: 606
 polymer and rubber antioxidant exposure, bladder cancer, Britain: 927
 OCCUPATIONAL DISEASES, (Contd.)
 silicosis, primary hemangioendothelial tumor of heart: 682
 skin cancer, epidemiology, Britain: 889
 OILS, EDIBLE
 margarine or chocolate, carcinogen content, processing methods, Germany: 604
 OILS, MINERAL (See also Petroleum)
 plasmacytoma, mammary tumor virus-like particles, mouse: 730
 OVARY NEOPLASMS
 familial (mother and daughters): 886
 induction, dimethylbenzanthracene, glucose oxidation in tumors, mouse: 649
 second primary tumor, risk, breast cancer, Connecticut: 909
 OXALACETIC ACID
 stimulation of tumor cells in vitro: 615
 PANCREAS NEOPLASMS
 epidemiology, chemists, U.S.: 933
 PERITONEUM
 mesothelioma, occupational asbestos exposure: 681
 PETROLEUM AND PETROLEUM PRODUCTS
 automobile exhaust, air pollution, USSR (rural): 735
 PHARYNX NEOPLASMS
 epidemiology, smoking and dietary factors, Puerto Rico: 932
 PHTHALATE DERIVATIVES
 mutagenesis and effect on tumor incidence, Drosophila: 626
 PITUITARY NEOPLASMS
 estrone-induced or spontaneous, plasma prolactin levels, rat: 728
 metastatic, frequency, breast and other cancer: 966
 prolactin-producing, radioimmunoassay of hormone, rat: 727
 PLANARIA
 methylcholanthrene, benzpyrene or benzanthracene tumors: 627
 PLASMACYTOMA (See under Myeloma and related diseases)
 PLEURA
 mesothelioma, occupational asbestos exposure: 681
 POLYANIONS
 effect on avian sarcoma viruses: 782
 POLYCATIONS
 effect on avian sarcoma viruses: 782
 POLYINOSINIC:POLYCYTIDYLIC ACID (See Nucleic acids, RNA, synthetic polymer)
 POLYMERS
 basic, induction of specific viral repressor, abortively or productively SV40-infected cells: 853
 POLYVINYLPYRIDINE N-OXIDE
 leukemia and mammary tumors, mouse or rat: 717
 PONCEAU MX (food coloring)
 liver toxicity, mouse: 609
 PREGNANCY
 cervix cancer
 Oklahoma (Oklahoma City): 906

PREGNANCY, (Contd.)

- Pennsylvania (Philadelphia): 907
- genital and mammary tumor induction, alkylnitrosoureas, rat: 713, 723
- normal or pathological, host immunity and hormonal feedback mechanism, human and animal: 967
- placental aryl hydrocarbon hydroxylase activity, smoking, human: 685
- transplacental tumor induction, rat: 634, 635, 637, 714

PROCARBAZINE (See under Antitumor agents)

PROSTATE NEOPLASMS

- induction, testosterone + methylcholanthrene, histochemistry, mouse: 716
- viral etiology, review: 576

PROTEINS

- bound dibenzanthracene metabolite, identification, mouse skin: 698
- dietary deficiency, liver cirrhosis and hepatoma, rat: 673
- liver, methyl dimethylaminoazobenzene hepatoma, rat: 651
- Rous sarcoma virus-infected cells with/without nuclear fragmentation: 795
- serum α 1-fetoprotein, dietary pyridoxine deficiency, primate: 970
- tyrosine-containing adenovirus-12-transformed hamster embryo cells: 839

PSYCHOKINESIS

- effect on exptl. tumors: 985

PYRIDOXINE

- dietary deficiency
- liver cancer epidemiology, Africa: 970
- serum α 1-fetoprotein, primate: 970

QUINOLINE, 4-HYDROXYAMINO-

- DNA inactivation, mechanism, bacteria: 616

QUINOLINE, 4-HYDROXYAMINO-, 1-OXIDE

- intracerebral implantation, induction of obesity, mouse: 620

QUINOLINE, N-NITROSO-2,2,4-TRIMETHYL-1,2-DIHYDRO-,

POLYMERIZED (rubber additive)

- s.c. tumors, rat: 606

RADIATION CARCINOGENESIS

- bone, child with retinoblastoma: 588
- sun exposure, melanoma, Australia, review: 558
- or radiotherapy, lupus vulgaris with malignant transformation: 595
- thyroid, Japan (Hiroshima/Nagasaki): 930

RADIATION EFFECTS

- adenovirus-31 transformation efficiency, hamster embryo cells: 846
- bone marrow chromosomes
- atomic radiation-exposed healthy subjects, Hiroshima: 591
- rat: 590
- cured tracheal cancer, second (esophagus) and third (prostate) primary tumors: 593
- exptl. tumors in vivo, mathematical model: 940
- fowl plague virus multiplication, singly- or doubly-infected cells: 780

RADIATION EFFECTS, (Contd.)

- mammary tumor virus activation, 020 strain mice: 818
- polyoma virus functions, cell cultures or hamster: 855, 856
- SV40 replication or transforming efficiency, cell cultures: 846, 857
- Yaba monkey poxvirus: 868

RADIATION LEUKEMOGENESIS

- atomic radiation (Hiroshima), bone marrow chromosomes: 592
- germ-free or conventional mice: 589
- human, review: 586
- radiotherapy for other diseases, Japan, review: 561

RESORCINOL

- mutagenesis and effect on tumor incidence, Drosophila: 626

RESPIRATORY NEOPLASMS

- epidemiology
- Italy (Genoa): 905
- occupational arsenic exposure, U.S.: 926
- multiple primary, smoking: 931

RESPIRATORY TRACT

- epithelial hyperplasia, smoking, chromosomes, human: 684
- toxicity
- beryllium ores, monkey or hamster: 678
- cigarette smoke, animal: 687
- human: 683

RETICULOENDOTHELIAL SYSTEM

- macrophages, age-related herpesvirus resistance, mouse: 876
- splenectomy and anticoagulants, effect on transplanted tumor, mouse: 622
- thymectomy, effect on virus-induced mammary nodule or tumor induction, mouse: 820, 821

RIFAMPICIN

- effect on sarcoma virus production and transformation, chick embryo cells: 794

RUBBER AND RUBBER ADDITIVES

- occupational exposure
- bladder cancer, Britain: 927
- cancer risk: 606
- s.c. tumors, rat: 606

SALMONELLOSIS

- effect on aflatoxin toxicity, chicken: 749

SCAR TISSUE (See also under Injury)

- lupus vulgaris, malignant transformation, sun exposure or radiotherapy: 595
- peptic ulcer, stomach cancer: 596, 939

SEX

- chromosomes
- genital, breast and other tumors, women: 955
- testicular teratomas from male or female embryo grafts, mouse: 957
- XY/XO mosaicism, with other chromosome abnormalities, acute myeloid leukemia: 954
- difference
- aflatoxin metabolism, rat: 668
- benzpyrene metabolism, liver microsomes, rat: 643

SUBJECT INDEX

- LICA
effect on herpesvirus infection, mouse: 875
- LICON
dust, occupational exposure, primary
hemangioendothelial tumor of heart: 682
- LIVER NITRATE
selective affinity of avian tumor viruses,
infected chicken cells: 783
- IN
proteins, bound dibenzanthracene metabolite,
analysis, mouse: 698
toxicity, aflatoxins, rabbit: 669
tobacco smoke condensate, human: 691
- IN CARCINOGENESIS
benzpyrene, tumor growth rates, mouse: 920
chlorinated benzpyrene derivatives, mouse:
602
dimethylbenzanthracene, hamster cheek pouch:
694, 695, 696, 697
estradiol, rat: 707
methylcholanthrene
rat: 707
effect of dimethylaminostilbene: 659
squirrel monkey: 700
s.c. sarcoma
antitumor agent (ibenzmethylin), rat: 605
dimethylbenzanthracene, germ-free mice: 611
methylcholanthrene
germ-free mice: 611
tumor-specific antigens, guinea pig or
mouse: 657, 658
nitroquinoline oxide, rat: 674
printing inks, mouse: 607
rubber additive, rat: 606
tobacco tar or smoke condensate, mouse:
688, 689, 692
- IN NEOPLASMS
eccrine sweat duct tumors, benign and malignant,
differentiation: 968
lupus vulgaris scars, sun exposure: 595
melanoma
nuclear RNA fractionation: 950
seasonal incidence, amphibian (*Triturus*):
628
sun exposure, Australia, review: 558
occupational, epidemiology, Britain: 889
preinvasive or malignant, mosaicism, human:
923
ulcus terebrans, classification: 988
- SL
anaerobic bacteria, benzpyrene synthesis: 600
- SUBIC ACID
effect on connective tissue, rat: 699
- SEEN
antibody localization, Moloney virus-induced
lymphoma, mouse: 770
Nase and RNase, effect of Friend leukemia
virus, mouse: 765
- STOMACH NEOPLASMS
epidemiology
mathematical models: 896
Poland: 897
iology, possible, nitrate reduction to
nitrosamine by gastric bacteria, human: 639
growth rate, role of intestinal metaplasia or
ulceration: 939
- STOMACH NEOPLASMS, (Contd.)
malignant transformation
of familial polyposis (Peutz-Jeghers),
child: 962
of peptic ulcer: 596, 939
- SULFATE ION
effect on hydroxyfluorenylacetamide metabolism,
rat liver: 672
- STILBENE, DIMETHYLAMINO-
skin tumors, effect on methylcholanthrene
carcinogenesis, rat: 659
- SV40 (See under Virus, papova)
- TEMPERATURE
effect on antigens and thymidine kinase,
SV40-infected cells: 874
high, inactivation of Yaba monkey poxvirus:
868
refrigeration, effect on aflatoxin production,
Aspergillus flavus: 661
- TESTIS NEOPLASMS
epidemiology, Denmark, urban and rural: 936
teratoma, from male or female embryo tissue
grafts, sex chromosomes, mouse: 957
- TESTOSTERONE
with methylcholanthrene, prostate tumors,
histochemistry, mouse: 716
- THALIDOMIDE
mutagenesis and effect on tumor incidence,
Drosophila: 626
- THIOURACIL, METHYL-
thyroid tumors, ultrastructure, hamster: 726
- THIOUREA
toxicity, lung, mouse: 701
- THYMINE ALKYLAMINE (See under Antitumor agents)
- THYROID NEOPLASMS
epidemiology
Israel: 883
Minnesota (Olmsted County; Rochester): 887
radiation exposure, Japan (Hiroshima/
Nagasaki): 930
review: 584
medullary carcinoma, with epinephrine-producing
pheochromocytoma, familial: 948
methylthiouracil-induced, ultrastructure,
hamster: 726
sarcomas, epidemiology, Italy: 913
- TOBACCO
Aspergillus cultures, aflatoxin production:
748
chewing, mouth cancer, India (rural): 935
cigarette or cigar tar, skin tumors, mouse:
692
heavy metal content (lead, cadmium, nickel):
686
- TOBACCO SMOKE
cigarette or cigar, effect on bronchus: 737
condensate, skin toxicity, human: 691
skin tumors, mouse: 688, 689
filtered or unfiltered, heavy metal content
(lead, cadmium, nickel): 686
inhalation, chronic toxicity, animal: 687
- TOBACCO SMOKING
bladder cancer: 690
consumption rates 1910-1965, Denmark: 936

TOBACCO SMOKING; (Contd.)

- esophagus cancer
 - Puerto Rico: 932
 - South Africa, ethnic groups: 928
- larynx cancer, Czechoslovakia: 881
- life expectancy, U.S. men: 900
- lung cancer
 - ABO blood groups: 904
 - review: 569, 574
 - South Africa, ethnic groups: 901, 928
- mouth cancer
 - India (rural): 935
 - Puerto Rico: 932
- multiple primary tumors of upper g.i. and respiratory tract: 931
- pharynx cancer, Puerto Rico: 932
- placental aryl hydrocarbon hydroxylase activity, human: 685
- respiratory epithelial hyperplasia or squamous metaplasia, human: 683, 684

o-TOLUIDINE

- lung or kidney tumors, fetal mouse: 714

TOLUIDINE BLUE (See under Dyes and stains)

TONGUE NEOPLASMS

- epidemiology, Canada, urban and rural: 895

TOXICITY

- aflatoxin
 - effect of salmonellosis, chicken: 749
 - farm animals, review: 572
 - liver, species difference, salmon or trout: 666
 - rat: 699, 740
 - skin, rabbit: 669
 - species difference, mechanism: 750
- beryllium ores, respiratory, monkey or hamster: 678
- carcinogenic antitumor agent (ibenzmethylin), hamster: 605
- dimethyl-p-phenylazoaniline, cockroach: 624
- 2-fluorenamine, cockroach: 624
- food coloring (Ponceau MX), liver, mouse: 609
- hexamethylenetetramine, mouse or rat: 608
- lead acetate, kidney, hamster: 720
- methylcholanthrene, cockroach: 624
- sorbic acid, connective tissue, rat: 699
- tobacco smoke, animal: 687
- human: 683, 691

TRACHEA NEOPLASMS

- radiation cure, second (esophagus) and third (prostate) primary tumors: 593

TRAUMA (See Injuries)

TRIAZINE, PHENYLDIMETHYL-

- peripheral nerve tumors, rat: 636

TRYPAN BLUE (See under Dyes and stains)

TRYPTOPHAN METABOLITES

- effect on DNase-II, cell-free system: 612
- excretion, bladder cancer: 690

ULCER, PEPTIC

- malignant transformation (stomach cancer), human: 596, 939

URETHAN

- activation of mammary tumor virus, mouse: 818
- effect on DNA and RNA, transplanted tumor or regenerating liver, mouse: 621

URETHAN, (Contd.)

- kidney tumors, fetal mouse: 714
- lung tumors
 - effect of Freund's adjuvant, mouse: 677
 - fetal mouse: 714
 - mouse: 701
- mammary tumors, mouse: 712
- melanoma of eye, rat: 629

URETHAN DERIVATIVES

- butyl carbamate, mammary tumors, mouse: 712

URETHAN, N-HYDROXY-

- melanoma of eye, rat: 629

UTERUS NEOPLASMS (See Corpus uteri neoplasms)

VAGINA NEOPLASMS

- induction, alkylnitrosoureas, pregnant rat: 713

VIRAL CARCINOGENESIS

- cervix or prostate, review: 576
- DNA-containing mammalian viruses, mechanism, infected or transformed cells: 835
- RNA and DNA viruses, mechanism, review: 577

VIRUS

- fowl plague, replication, effect of irradiation or actinomycin, singly- or doubly-infected chick or hamster embryo cells: 780
- hepatitis (Mol; human), synergism with diethylnitrosamine, hepatoma, mouse: 653
- human lymphosarcoma cell line: 978
- possible human tumor virus, cellular antibodies against HeLa cell antigen, human carcinomas: 751

reo

- infection, associated with Gross-AKR type leukemia virus infection, mouse: 757
- intracellular membrane systems, Rous sarcoma virus-induced hamster tumors: 758

Sendai

- irradiated, SV40 rescue, mixed mouse kidney-transformed mouse cell cultures: 852
- Rous sarcoma virus rescue, mixed chick embryo-transformed hamster cell cultures: 786

- superinfection of tumors: 869

- Type A and Type C particles, spontaneously transformed mouse or rat embryo cells: 981

VIRUS, ADENO-

CELO (avian)

- transformed human cells, hamster tumors: 833

- oncogenic or nononcogenic, cytopathic effects, animal kidney cells: 872

SV11 (simian)

- transformation (*in vitro*) and tumor induction (*in vivo*), hamster: 844

type 2

- infected or transformed cells, virus-specific cellular RNA and viral DNA: 835

type 5

- infected hamster cells, thymidine kinase: 836

type 7

- serum antibodies, nasopharynx cancer, Hong Kong: 825

RUS, ADENO- (Contd.)

- type 12
 - group-specific T antigen, properties: 838
 - hamster tumors
 - effect of phage or synthetic RNA: 840
 - fetal or newborn hamster: 873
 - tumor mitochondria-specific antigen: 788
 - induction of cellular DNA, human embryo cells: 837
 - serum antibodies, nasopharynx cancer, Hong Kong: 825
 - transformed hamster embryo cells, DNA, RNA and tyrosine-containing proteins: 839
- type 18
 - serum antibodies, human cancer: 834
- type 31
 - transforming efficiency, radiation effects, hamster embryo cells: 846
 - tumor-specific transplantation immunity, hamster: 845
- US, HERPES
 - herpes simplex, persistent infection, mechanism, hamster cells: 824
 - infection, age-related resistance, role of macrophages, mouse: 876
 - effect of silica or immune serum, mouse: 875
 - pre malignant lip neoplasms: 594
- JS, HERPES-TYPE
 - Epstein-Barr (human)
 - Burkitt lymphoma and other human tumor cells: 827, 828, 829, 830, 831
 - serum antibodies, Burkitt lymphoma: 826
 - nasopharynx cancer: 825, 826, 925
 - larynx's disease (chicken)
 - isolation and properties: 877
 - strain HPRS-16, attenuation, chicken kidney cells: 832
- S, LEUKEMIA/LYMPHOMA
 - and C-type particles, cell-transmitted mouse leukemia: 756
- KR (mouse)
 - isolation, lymphoma (2731/L) from reovirus-infected mouse: 757
 - transmission, effect of germ-free status: 755
- animal, leukemia epidemiology, review: 578
- avian leukosis
 - latent, detection, chick embryo cells: 793
 - particles resembling, calf kidney cell line: 752
 - properties: 870
- avian myeloblastosis
 - effect on Rous sarcoma virus production, chicken: 792
- avian myelomatosis
 - detection, chick cells: 783
- strain A (avian myeloblastosis)
 - effect on fowl plague virus replication, chick embryo cells: 780
- group-specific antigen, chicken: 777
- induction of tumor-specific transplantation antigens to Rous virus tumors, mouse: 789

VIRUS, LEUKEMIA/LYMPHOMA, (Contd.)

- rabbit antibody complex, properties: 778
- chick erythroblastosis
 - induction of erythroblastosis or erythro-leukemia, rat: 754
- feline leukemia virus
 - C-type particles, myeloproliferative disorders, cat: 761
 - propagation, human embryo cells: 760
- Friend (mouse)
 - effect on splenic DNase and RNase, mouse: 765
 - immunosuppression, mouse: 766
 - infected mouse cells, effect of synthetic RNA polymer: 843
 - rat tumors, host immunity, rat: 764
 - leukemogenesis, effect of synthetic RNA polymer, mouse: 841
 - recovery (non-infectious reticulum cell sarcoma), Moloney leukemia virus as helper: 769
 - tumor inhibition by dimethylbenzanthracene, mouse: 617
- Graffi (mouse)
 - comparison of viral (structural) and cellular antigens: 762
 - isolation, spontaneous mouse sarcoma (RAB-1): 813
 - mouse lymphoma cells (GiC2 lymphoma), cellular antigens: 762
- Gross (mouse)
 - infected mouse cells, effect of synthetic RNA polymer: 843
 - isolation, lymphoma (2731/L) from reovirus-infected mouse: 757
 - transplantable lymphomas, syngeneic skin-graft rejection: 763
- 9H rat leukemia virus
 - properties, heterogeneous virus population, rat embryo cells: 759
- human, leukemia epidemiology, review: 578, 586
- MC29 (avian leukosis)
 - effect on chicken bone marrow cells: 779
- Moloney (mouse)
 - comparison of viral (structural) and cellular antigens: 762
 - effect on DNA and RNA, mouse embryo cells: 806
 - genetic susceptibility, role of hairless (hr) locus: 919
 - helper virus, recovery of Friend virus from non-infectious tumor: 769
 - infection, rescue of Moloney sarcoma virus from rat tumor (MSB-1), mouse: 804
 - infection and transmission, germ-free mice, review: 575
 - lymphoma antibodies, spleen, tumor-bearing mice: 770
 - mouse lymphoma cells (YC2 lymphoma), cellular antigens: 762
 - particles resembling, calf kidney cell line: 752
- RT34 rat strain, serum IgG, rat: 768
- ultrastructure, review: 579

VIRUS, LEUKEMIA/LYMPHOMA, (Contd.)

- mouse erythroblastosis (MEV)
 - rat-adapted, extrathymic lymphomas, rat: 753
- particles resembling, strain-specific immunity disorders, NZB mice: 871
- possible latent leukemia virus, high-plasma cell tumor mouse strain: 973
- Rauscher (mouse)
 - combined with diethylnitrosamine, trans-formation, rat embryo cells: 776
 - induction of myelofibrosis with leukemia or lymphosarcoma, rat: 772
 - infected mouse cells, effect of synthetic RNA polymer: 843
 - leukemia growth pattern, mouse: 775
 - strain difference in susceptibility, mouse: 774
 - tumor pathology, mouse and rat: 771
 - virus-induced host immunity to syngeneic or allogeneic tumor cells, mouse: 773

VIRUS, MAMMARY TUMOR

- mouse
 - absence of interferon-inducing or hemagglutinin activity: 823
 - activation, radiation or urethan, 020 strain mice: 818
 - effect on hyperplastic alveolar nodules: 819
 - infection and transmission, germ-free mice, review: 575
 - nodule and tumor induction, effect of thymectomy: 820, 821
 - nodule-inducing virus, effect on hyperplastic alveolar nodules: 819
 - particles resembling, calf kidney cell line: 752
 - replication cycle (milk or mammary tumors), ultrastructure: 816, 817
 - Type A particles, mineral oil-induced plasmacytoma: 730
 - Type B particles, methylcholanthrene-induced endymboblastoma, mouse: 822

VIRUS, PAPOVA (papilloma-polyoma-vacuolating)

- polyoma
 - alkaline degradation patterns: 860
 - CET strain and derivative (RTT) after mouse kidney passage, comparison: 863
 - DNA, non-infectious supercoiled type: 861
 - hamster tumor
 - glycoprotein distribution: 862
 - induction, radiation effects: 855, 856
 - host immunity, induction, antilymphocyte serum, mouse: 864
 - infectivity, radiation effects, mouse cells: 855
 - kidney sarcoma, growth pattern, rat: 866
 - LID-1 VR 252 strain, host immunity and tumor development, hamster or mouse: 865
 - rabbit fibrosarcoma cell lines, properties: 867
 - Rowe strain, hamster tumor extract, specific polyoma virus repressor: 854
 - transformed cells, genotypic and phenotypic changes, review: 580

SV40

- DNA, transformation, human cells: 851
- hamster tumors

VIRUS, PAPOVA (papilloma-polyoma-vacuolating) Contd

- cellular immunity: 850
- host immunity: 845, 850
- induction, effect of synthetic RNA polymer: 842
- tumor mitochondria-specific antigen: 788
- immunosuppressive effect, hamster: 767
- infected cells
 - localization of T antigen: 849
 - temperature sensitivity: 874
- replication
 - effect of repressor from polyoma virus-induced hamster tumor, monkey cells: 854
 - radiation effects, monkey kidney cells: 857
- rescue (irradiated Sendai virus), mixed transformed mouse-monkey kidney cell cultures: 852
- specific repressor, abortively or productively infected cells: 853
- transformation, methods of enhancement, hamster embryo cells: 846
- transformed cells
 - genotypic and phenotypic changes, review: 580
 - hamster embryo, variants: 859
 - human amnion, medium effects on cell growth: 847
 - new antigens: 848
 - reversion after *in vivo* propagation (hamster tumors): 858

VIRUS, POX

- vaccinia
 - reactivation of Yaba monkey virus: 868
- Yaba histiocytoma (monkey)
 - inactivation (heat or UV) and reactivation (vaccinia virus): 868

VIRUS, SARCOMA

- avian
 - subgroups B, C and D, effect of polyanions and polycations: 782
 - subgroups C and D, properties and classification: 781
- FBJ osteosarcoma (mouse)
 - classification: 814
 - infection, hamster or rat: 814
 - tumor induction, strain differences, mouse: 814
- Graffi pseudotype (mouse)
 - comparison of viral (structural) and cellular antigens: 762
- hamster-specific
 - C-type virus, isolation, Moloney (Gross pseudotype) sarcoma virus-induced hamster tumor: 802
 - isolation, hamster tumor induced by Kirsten (mouse) sarcoma virus: 801
- Harvey (mouse)
 - osteosarcoma, hamster or rat: 811
 - transformation, quantitation, hamster embryo cells: 809
 - transformed cells, mouse embryo, morphology: 810
- Kirsten (mouse)
 - hamster-specific virus, isolation, hamster sarcoma: 801

RUS, SARCOMA, (Contd.)

- transformed human cells, properties: 812
- Moloney (mouse)
 - competent and defective populations, isolation and properties: 807
 - effect on DNA and RNA, mouse embryo cells: 806
- Gross pseudotype, hamster tumor, hamster-specific sarcoma virus: 802
- immunotherapy and chemotherapy of tumors: 808
- infected cells, loss of interferon response, mechanism: 805
- osteosarcoma, hamster or rat: 811
- rescue from rat tumor (MSB-1), Moloney leukemia virus-infected mouse: 804
- transformation
 - effect of antitumor antibiotics, role of cellular DNA and RNA, mouse embryo cells: 803
 - quantitation, hamster embryo cells: 809
- transformed cells
 - human, properties: 812
 - mouse embryo, morphology: 810
- Moloney pseudotype (mouse)
 - comparison of viral (structural) and cellular antigens: 762
- mouse
 - effect of synthetic RNA polymer, mouse embryo cells: 843
- particles resembling
 - human bone or soft tissue sarcoma cultures: 815
- Rauscher pseudotype (mouse)
 - transformation, quantitation, hamster embryo cells: 809
- Rous (chicken)
 - Bryan strain
 - hamster tumors, reovirus particles: 758
 - nonviral growth-stimulating factor in medium, chick embryo cells: 791
 - phenotypically mixed populations: 785
 - effect of rifampicin, chick embryo cells: 794
 - hamster tumors, host immunity: 800
 - infected chick embryo cells, nuclear fragmentation: 795
 - latent infection, detection, chick embryo cells: 793
 - particles resembling, calf kidney cell line: 752
 - Prague strain
 - group-specific antigen components, infected cells: 777
 - RNA, possible subunit structure: 784

VIRUS, SARCOMA, (Contd.)

- RSV (RAV-1) pseudotype
 - phenotypically mixed populations: 785
- Schmidt-Ruppin strain
 - brain tumor, antibody localization, dog: 797
 - chick cells: 783
 - enhanced virus production, chicken: 792
 - group-specific antigen components, infected cells: 777
 - hamster tumor, long-term cultivation: 799
 - kinetics of Type A and C particle development, transformed chicken cells: 787
 - mouse tumor (SR-C3H/He sarcoma), tumor mitochondria-specific antigen: 788
 - rescue (Sendai virus), mixed chick embryo-transformed hamster cell cultures: 786
 - soft tissue or bone sarcomas, marmoset: 798
 - tumor induction, germ-free rat: 790
- transformed cells
 - effect of nitrogen mustard derivative, rat: 796
 - hamster embryo, fowl plague virus multiplication, cellular DNA: 780
 - tumor-specific transplantation antigens, induction, avian myeloblastosis virus, mouse: 789
- type 0, effect of polyanions and polycations: 782
- Rous-associated virus (RAV-1)
 - Bryan high-titer strain (chicken), detection, chick cells: 783
 - group-specific antigen, multiple components, chick embryo cells: 777
- Rous-interference factor (chicken)
 - detection of latent avian leukosis virus infection, chick embryo cells: 793
 - serum antibodies, sarcoma pts. and their relatives: 815
- VITAMIN A PALMITATE
 - effect on dimethylbenzanthracene cheek pouch tumors, hamster: 694
- WATER SUPPLY
 - chlorination, screening of chlorinated benzpyrene derivatives, mouse: 602
- XANTHINE, 3-HYDROXY-
 - effect on DNase-II, cell-free system: 612
 - urinary metabolites, rat: 618



U.S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
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Vet. Med.

JUNE-JULY 1970

Abstract Nos. 990-1435

Vol. 8

No. 6-7

CARCINOGENESIS ABSTRACTS

National Cancer Institute

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE • National Institutes of Health

CARCINOGENESIS ABSTRACTS

Volume 8, Numbers 6,7

Abstract Numbers
990-1435

CONTENTS

	<u>Page</u>
view	199
ysical Carcinogenesis	204
emical Carcinogenesis	208
ra] Carcinogenesis	239
idemiology and Biometry	258
scellaneous	271
thor Index	i
bject Index	vi

Prepared by Scientific Literature Corporation
Philadelphia, Pennsylvania 19103

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Persuant to a Contract with the Public Health Service
U.S. Department of Health, Education and Welfare
PH43-70-2036

Use of funds for printing this publication approved
by the Director of the Bureau of the Budget on July 25, 1967.

FOREWORD

The National Cancer Institute, in response to Congressional interest and desire for a national program of cooperative research in cancer, is establishing a means whereby information in the field of carcinogenesis will be coordinated and made available. The information to be included will be obtained from the National Cancer Institute, other governmental agencies, and non-governmental research institutions.

The issuing of Carcinogenesis Abstracts under the auspices of the National Cancer Institute will provide a central source for current abstracting of the carcinogenesis literature being published throughout the world. This will help facilitate an integrated and cooperative program of investigation in this area. The growing number of publications in the area of carcinogenesis makes imperative the availability of an appropriate abstracting service so that investigators may be apprised of progress with a minimum of delay. It is our desire to provide the investigator with a readily systematized compilation of the published work.

Carcinogenesis Abstracts will be published monthly and will include abstracts from the most recently published literature.

Inquiries may be addressed as follows:

Carcinogenesis Abstracts
National Institutes of Health
National Cancer Institute
Bethesda, Maryland 20014

NOTE

Journal names are abbreviated according to the list of abbreviations used by Index Medicus. If the journal is not covered by Index Medicus, then the abbreviations (with some modifications) found in World Medical Periodicals, 3rd Edition, are used.

ABBREVIATIONS USED IN ABSTRACTS

admin.	administered, administration	mg	milligram(s)
av.	average	min.	minute(s)
C	curie(s)	ml	milliliter(s)
mC	millicurie(s)	mm	millimeter(s)
C	microcurie(s)	mo.	month(s)
m	centimeter(s)	MTD	maximum tolerated dose
onc.	concentration	NIH	National Institutes of Health, USA
pm	counts per minute	p.o.	orally
NA	deoxyribonucleic acid	QO2	oxygen quotient
Nase	deoxyribonuclease	PFU	plaque forming unit
g.	for example	ppm	parts per million
FU	focus forming unit	pt.(s)	patient(s)
.i.	gastrointestinal	RBC	red blood cells (erythrocytes)
	gram(s)	RES	reticuloendothelial system
g	microgram(s)	resp.	respectively
b	hemoglobin	RNA	ribonucleic acid
.a.	intra-arterial	RNase	ribonuclease
D50	median infectious dose	soln.	solution
nj.	injected, injection(s)	s.c.	subcutaneous
noc.	inoculated, inoculation(s)	TCID	tissue culture infectious dose
.p.	intraperitoneal	x	times (e.g. x 3/wk.)
.U.	international unit(s)	U	unit
.v.	intravenous	UV	ultraviolet
g	kilogram(s)	vol.	volume
D50	median lethal dose	VA	Veterans Administration
	molar, mole(s)	wt.	weight
1	millimole(s)	WBC	white blood cells (leukocytes) or white blood cell count
1	micromole(s)	yr.	year(s)
ix.	maximum		

LANGUAGE ABBREVIATIONS

Afrikaans	E.	English	Hun.	Hungarian	Lith.	Lithuanian	Ser.	Serbo-Croatian
Arabic	Eston.	Estonian	lc.	Icelandic	Maced.	Macedonian	Sl.	Slovene
Bulgarian	Fin.	Finnish	ln.	Indonesian	Nor.	Norwegian	Sp.	Spanish
Chinese	Fr.	French	It.	Italian	Pol.	Polish	Sw.	Swedish
Czech	Ger.	German	Jap.	Japanese	Por.	Portuguese	Th.	Thai
Danish	Gr.	Greek	Kor.	Korean	Rum.	Rumanian	Uk.	Ukrainian
Dutch	Heb.	Hebrew	Latv.	Latvian	Rus.	Russian	Viet.	Vietnamese

- 70-990 TUMORS OF THE BUCCAL CAVITY. (It.) Balli, L. (City Hosp., Rimini, Italy), B. Vernole and F. Cavazzuti. Minerva Med. 60(70):3202-3213, 1969. (106 references)

A review includes sections on the diagnosis, differential diagnosis, prognosis and treatment of malignant tumors of the lip, cheek, gum, tongue, hard and soft palates, and floor of the mouth. The need for regular, exfoliative cytologic examination is emphasized for persons engaged in activities predisposing to the development of this type of tumor.

- 70-991 THE SIGNIFICANCE OF THE THYMUS FOR TUMOR DEVELOPMENT AND LEUKEMOGENESIS. (Ger.) Klug, H. (U. Berlin Charity Derm. Clin.). Deutsch. Gesundh. 24(8):337-346, 1969. (168 references)

A discussion and review of the thymus as a "primary immunity organ." The possible significance of lymph follicles (which are found in the thymus in myasthenia gravis, Basedow's disease, or struma diffusa) and of plasma cells (which are increased in myasthenia gravis, lupus erythematosus and aplastic anemia) for the production of antibodies and autoantibodies is stressed. The tumor-inhibiting effect of the thymus (especially pronounced with tumors induced by polyoma, SV40 and adenovirus type 12) seems to be related to its immunological function. On the other hand it has a leukemogenesis-stimulating effect since the development of lymphatic leukemia in mice depends on the presence of the thymus. Leukemogenesis can be prevented in highly susceptible strains by thymectomy and sensitivity to leukemia restored by reimplantation of the thymus.

- 70-992 BRAIN TUMORS: THEIR INCIDENCE AND CLASSIFICATION IN MAN AND THEIR EXPERIMENTAL PRODUCTION. (E.) Zimmerman, H. M. (Albert Einstein Coll. Med., Bronx, N. Y.). Ann. NY Acad. Sci. 159(2):337-359, 1969. (21 references)

Incidence and classification of different series of cases of intracranial tumors were compared, with special emphasis on the human gliomas. The experimental induction of tumors by hydrocarbons (methylcholanthrene, dibenzanthracene and benzpyrene), their histology, and metastasis were discussed specifically concerning ependymomas, glioblastoma multiforme, oligodendroglioma, polar spongioblastoma, mixed gliomas, astrocytomas and medulloblastomas. The carcinogenic activity of virus-like particles found in chemically-induced precancerous lesions is discussed.

- 70-993 THE IMMEDIATE RESPONSE OF BLADDER EPITHELIUM TO INJURY BY CHEMICAL

- CARCINOGENS. (E.) Clayson, D. B. (Sch. Med., Leeds, England) and E. H. Cooper. Brit. J. Urol. 41(6):710-713, 1969. (7 references)

After a single dose of 0.5 mg 4-ethylsulfonyl-naphthalene-1-sulfonamide (ENS) p.o., mouse bladder epithelium exhibited increased DNA and RNA synthesis following a latent period of about 18 hr. The cells at all levels of the epithelium took part in the proliferation and the interval between successive mitoses in diploid and tetraploid cells was identical. However, when ENS was admin. by continuous feeding of 0.01% for 9 weeks, almost all the epithelial cells became diploid and the proliferative response was much less. Alkaline phosphatase, normally in the basal and intermediate cell layers, is not detectable after feeding with ENS. In the epithelization of the mouse bladder after denudation with an oral dose of cyclophosphamide, the diploid cells initiated the proliferative response and, occasionally, large cells containing high quantities of DNA were produced.

- 70-994 FLUOROPHOTOGRAPHY AND CONVENTIONAL RADIOLOGIC STUDIES IN THE DIAGNOSIS OF PULMONARY TUMORS. (It.) De Albertis, P. (Via De Gaspari 1/16, Genoa, Italy). Radiol. Med. (Torino) 50(6):513-525, 1969. (17 references)

A review of the value and costs of fluorophotography as an adjunct to conventional chest X-ray techniques in the mass screening of presumably healthy populations includes a preliminary report of a survey being conducted by the Tyrrhenian Maritime Health Service in Genoa. In addition to confirming tuberculous and other thoracic complications in an unspecified number of some 69,000 sailors who were screened before embarking from that port, presymptomatic, primary pulmonary neoplasms were found in 4 subjects.

- 70-995 GNOTOBIOTES AS USEFUL TOOLS IN STUDIES IN CARCINOGENESIS WITH CYCASIN, A NATURAL GLUCOSIDE. (E.) Laqueur, G. L. (NIH, Bethesda, Md.). Adv. Exp. Med. Biol. 3:163-167, 1969. (11 references)

A review is made of the use of gnotobiotes in determining whether the toxicity and oncogenicity of cycasin in rats is due to β -glucosidase activity of the intestinal tract. Germfree rats, fed cycasin, suffered no ill effects and did not excrete methylazoxymethanol (MAM), a toxic metabolite of cycasin. Monocontamination of the germfree animals with bacteria having β -glucosidase activity hydrolyzed cycasin to MAM in proportion to the contaminants' enzyme activity. Finally, MAM produced tumors in germfree and conventional rats independent of the route of administration.

- 70-996 A SURVEY OF METAL CARCINOGENESIS. (E.)
Furst, A. (U. San Francisco Inst. Chem.
Biol., Calif.) and R. T. Haro. Progr. Exp.
Tumor Res. 12:102-133, 1969. (170 references)

The association of trace elements with various neoplastic conditions is discussed and a review presented of metals reported to be carcinogenic, including magnesium (atomic numbers 12 and 25), aluminum, titanium, chromium, iron, cobalt, nickel, copper, zinc, arsenic, selenium, silver, cadmium, gold, mercury, tin, lead and asbestos. Several populations at risk are mentioned.

- 70-997 STUDIES ON THE MECHANISM OF ACTIVATION
OF AROMATIC AMINE AND AMIDE CARCINOGENS
TO ULTIMATE CARCINOGENIC ELECTROPHILIC REACTANTS.
(E.) Miller, E. C. (U. Wisconsin Med. Ctr.
McArdle Lab., Madison) and J. A. Miller. Ann. NY
Acad. Sci. 163(2):731-750, 1969. (61 references)

The N-hydroxylation and N-hydroxy esterification of N-hydroxy-2-acetylaminofluorene is discussed in relation to *in vivo* activation of aromatic amine and amide compounds to carcinogens. Metabolic conversion to a compound with electrophilic properties is ascribed to most chemical carcinogens including nitrosamines, azo compounds, ethionine and cycasin. The targets of the carcinogenic electrophilic reactants seem to be the bases of the nucleic acids and certain protein-bound amino acids.

- 70-998 IN VIVO REACTIONS OF NITROSO COMPOUNDS.
(E.) Magee, P. N. (Middlesex Hosp.
Med. Sch., London). Ann. NY Acad. Sci. 163(2):
717-729, 1969. (81 references)

The biological action of N-alkylnitroso compounds is discussed in relation to acute cellular injury to the liver and other organs, carcinogenesis, mutagenesis, and teratogenesis. Specificity of action, the nature of the biologically active intermediates, and the intracellular sites of action are also reviewed along with the occurrence of nitroso compounds in the environment.

- 70-999 CARCINOGENIC EFFECTS OF STEROIDS. (E.)
Bischoff, F. (Santa Barbara Cottage
Hosp. Res. Inst., Calif.). Advances Lipid Res.
7:165-244, 1969. (341 references)

Neoplasms induced by steroid hormones are reviewed, including estrone-dependent rat adrenal cortex carcinoma, anterior lobe chromophobe adenoma, endometrial neoplasm in rodents, interstitial cell tumors, local sarcomas, tumors of lymphocyte, monocyte and myeloid cell origin, uterine-vaginal and granulosa-cell ovarian tumors. Carcinogenic effects of cholesterol and its derivatives are also reviewed, and the etiology and treatment of endocrine-linked neoplasms in humans discussed.

- 70-1000 TOXICOLOGIC ASPECTS OF THE N-HYDROXYLA-
TION OF AROMATIC AMINES. (Ger.)
Uehleke, H. (U. Tubingen Pharmacol. Inst.,
Germany). Naunyn Schmiedeberg. Arch. Pharm.
263(1):106-120, 1969. (60 references)

A review includes sections on the biochemistry of N-hydroxylation, the role of the aromatic amines in the formation of methemoglobin, allergic reactions induced by the binding of aromatic amine groups to protein, the aromatic amines and polyneuropathies, and the carcinogenic activity of the aromatic amines.

- 70-1001 CARCINOGENIC EPOXIDES, LACTONES, AND
HALO-ETHERS AND THEIR MODE OF ACTION.
(E.) Van Duuren, B. L. (New York U. Med. Ctr.
Inst. Environ. Med. N. Y.). Ann. NY Acad. Sci.
163(2):633-650, 1969. (48 references)

The carcinogenicity and routes of admin. in rats and mice of epoxides (mono, di, and polyfunctional), beta- and gamma-lactones, and halo-ethers are reviewed. Emphasis is placed on the structural-activity relationships, and the carcinogenic action due to cross-linking or point mutations of DNA, alkylation of nucleoprotein, and intercalation between base pairs is discussed. Alkylating agents were tested and found to be less potent than dimethylbenzanthracene as initiating agents, using phorbol ester as a promoting agent. Carcinogenicity, mutagenicity, and tumor-initiating activity are compared to other compounds.

- 70-1002 COMPARISON OF CHEMICALLY INDUCED AND
VIRUS-INDUCED CHROMOSOME ABERRATIONS.
(E.) Nichols, W. W. (Inst. Med. Res., Camden,
N. J.). Fed Proc. 28(6):1794-1796, 1969.
(13 references)

Chromosomal damage induced by viruses was divided into 3 types of visible changes described as single breaks, severe fragmentation or chromosomal pulverization, or involving the spindle to produce changes in the chromosome number and segregation. The first 2 of these changes are compared to chemically-induced aberrations which interfere with or inhibit cellular DNA synthesis and produce breaks which are morphologically identical to those produced by virus, and chemicals which interfere with cellular protein synthesis, which may have a similar mechanism of action as virus. Other possible mechanisms of action are mentioned.

- 70-1003 BIOLOGICAL SIGNIFICANCE OF INDUCED
HUMAN CHROMOSOME ABERRATIONS. (E.)
Nowell, P. C. (U. Pennsylvania Sch. Med.,
Philadelphia). Fed Proc. 28(6):1797-1803, 1969.
(61 references)

Chromosomal aberrations caused by irradiation, chemicals or virus are discussed in relation to neoplastic disease, immunological disorders and the aging process.

70-1004 CANCER OF THE NASOPHARYNX. (E.)
Schoental, R. (Med. Res. Council Labs.,
Carshalton, Surrey, England). Cancer Res. 30(1):
252, 1970. (10 references)

Sinapylaldehyde (3,5-dimethoxy-4-hydroxycinnamal-
dehyde) has been correlated with nasopharyngeal
tumors in China, where it is a component of
Chinese incense smoke derived from sandalwood,
and in the Highlands of Kenya, where its conc.
is high in eucalyptus wood. Since these studies,
a high incidence of adenocarcinoma of the nasal
sinuses has been found among furniture workers
of England, Holland and France, possibly related
to these α,β -unsaturated aldehydes.

70-1005 N-NITROSO COMPOUNDS IN ORGANOTROPIC AND
TRANSPLENTAL CARCINOGENESIS. (E.)
Bruckrey, H. (Max Planck Inst. Immunobiol.,
Freiburg, Germany), R. Preussmann and S. Ivankovic.
Ann. NY Acad. Sci. 163(2):676-695, 1969.
(63 references)

The organospecific carcinogenic activity of
dialkylnitrosamines, acylalkylnitrosamides, and
diazo compounds was tested in adult rats and
guinea pigs, along with the transplacental
carcinogenicity of ethylnitrosourea and dialkyl-
nitrosamines in prenatal animals. All tumors
produced were histologically and grossly similar
to the corresponding human tumors. Mechanisms
of action and relationship to cancer prevention
are discussed.

70-1006 CELL TRANSFORMATION AND THE GENESIS OF
CANCER. (E.) Bendich, A. (410 E. 68
St., New York, N. Y.), E. Borenfreund, Y. Honda
and M. Steinglass. Arch. Environ. Health
(Chicago) 19(2):157-166, 1969. (46 references)

The patterns of growth of normal and transformed
cells are compared in relation to contact
inhibition and the formation of intracellular
bridges. Autoradiographic methods and immuno-
fluorescent studies have shown that when mouse
Ehrlich acites tumor cells and normal Chinese
hamster cells are incubated together, DNA is
transferred from the tumor cell to the Chinese
hamster cell by means of intracellular bridges,
but not in reverse. There is a similar relationship
between Syrian hamster cells and L-5178 mouse
leukemia cells. Chinese hamster cells incubated
with DNA from Ehrlich acites cells may have
produced a mouse DNA-specified antigen and were
able to grow in vivo as tumors.

70-1007 SUITABILITY OF CELL CULTURES FOR
CARCINOGENICITY TESTS. (E.) Schindler,
(U. Bern, Switzerland). Food Cosmet. Toxic.
(London) 7:233-237, 1969. (39 references)

The use of cell cultures as a test system for
carcinogenicity of chemicals is discussed

and transformation contrasted with neoplastic
change. The ability of certain chemicals to
induce cellular transformation is briefly
described.

70-1008 INHIBITION OF TUMORIGENESIS. (E.)
Van Duuren, B. L. (New York U. Med.
Ctr. Inst. Environ. Med., N. Y.) and S.
Melchionne. Progr. Exp. Tumor Res. 12:55-94,
1969. (101 references)

A review of biochemical and biological studies
on the mode of action of various anticarcinogens
inhibiting tumor induction in a number of test
systems including liver, mammary and skin car-
cinogenesis in mice and rats. Mechanisms dis-
cussed are the inhibition of synthesis of intra-
cellular constituents, induction of microsomal
enzymes, competition for intracellular sites and
several unknown modes of action.

70-1009 TRANSPLANTATION ANTIGENS AND VIRAL
CARCINOGENESIS. (E.) Haughton, G.
(U. North Carolina Sch. Med., Chapel Hill) and
D. R. Nash. Progr. Med. Virol. 11:248-306, 1969.
(227 references)

The genetics, biochemistry, and biology of
normal transplantation antigens in the human,
rat and mouse is discussed. Antigenic change
in tumors is also reviewed, including tumor-
specific transplantation antigens of virally,
chemically and radiation-induced tumors; the
thymus-leukemia antigens and tumor virus
antigens which have not been proven to be
transplantation antigens; and antigens not
proven or tested as transplantation antigens
such as the growth-associated and Burkitt's
lymphoma antigen. The antigens lost from
tumors, methods of detecting and measuring
tumor-specific antigens, and the relationship
between tumor-specific and normal transplantation
antigens are also discussed.

70-1010 RECENT ADVANCES IN MOLECULAR PATHOLOGY:
A REVIEW. SOME ASPECTS OF CHROMOSOME
CHANGES IN CANCER. (E.) Porter, I. H. (Birth
Defects Inst., Albany, N. Y.), W. F. Benedict,
C. D. Brown and B. Paul. Exp. Molec. Path.
(London) 11(3):340-367, 1969. (110 references)

Marker chromosomes are examined in order to
relate specific chromosomal changes to various
cancers. The Philadelphia chromosome and a long
acrocentric marker, which has been associated
with cancer in all 3 germ layers, are discussed
in detail, and more briefly, the Christchurch
chromosome, a long submetacentric chromosome
associated with cancer of the ovary, testis
and bronchus, the Api chromosome and carcinoma
of the cervix, the Melbourne chromosome and
lymphomas, and markers associated with

Waldenström's macroglobulinemia and Ewing's tumor. Neoplastic proliferation stemming from a chromosomal aberration was correlated in the case of virally-induced transformation and the high frequency of cancer and chromosomal abnormalities in Bloom's disease, Fanconi's syndrome, ataxia-telangiectasia and Down's syndrome.

70-1011 CONSEQUENCES OF ALKYLATION FOR THE BEHAVIOR OF DNA. (E.) Strauss, B. (U. Chicago, Ill.), M. Coyle and M. Robbins. Ann. NY Acad. Sci. 163(2):765-786, 1969. (45 references)

The reaction of DNA with monofunctional alkylating agents had been found to produce DNA with methylated bases, which can participate in bacterial transformation, and with single-strand breaks, which cannot. Bacterial or mammalian cell extracts contain an endonuclease which may produce breaks at or near the site of methylated bases, but some of the bases appear to be resistant. Breaks caused by both alkylation or by endonuclease may be repaired by bacterial or animal cell systems, but the resistant methyl groups may escape the repair system and serve as sites of mutagenesis.

70-1012 CYTOTROPISM OF LEUKEMIA VIRUSES. (E.) Dougherty, R. M. (State U. New York Upstate Med. Ctr., Syracuse) and H. S. Di Stefano. Progr. Med. Virol. 11:154-184, 1969. (81 references)

Various methods of study used to detect virus in animal tissue are reviewed and a classification presented of cells that support viral multiplication in chickens infected with avian leukosis viruses and in rodents infected with murine leukemia viruses. The origin of viremia, extent of cytotropism and interpretation of negative findings are also described. Finally, there is a discussion of contact and congenital transmission of virus, the relationship of cell activity to virus synthesis, and the cell response.

70-1013 BIOLOGICAL AGING, PHYSIOLOGICAL CYCLE, AND CARCINOGENESIS. (E.) Chook, E. K. (U. California Sch. Public Health, Berkeley). Gerontologist 9(4):296-299, 1969. (26 references)

The genetic composition of an individual includes a "biological clock" with a fixed speed which pre-determines the life-span, but which may be accelerated possibly by the accumulation of somatic mutations caused by environmental factors such as irradiation, viruses chemicals, etc. The breakdown of the regulatory cycle of the hematopoietic system in leukemia is discussed and the impairment of immunologic resistance, which is dependent on the physiologic condition of the host and thus decreases with age, is

correlated with the greatly increased incidence of cancer with age.

70-1014 FOOD CONTAMINANTS AND GASTROINTESTINAL OR LIVER NEOPLASIA. SURVEY OF EXPERIMENTAL OBSERVATIONS. (E.) Kraybill, H. F. (Food Drug Admin., Washington, D. C.). Environ. Res. 2(4):231-246, 1969. (72 references)

The level of carcinogens contained in various foods as a result of processing is discussed including the polycyclic hydrocarbon content of roasted coffee, smoked foods and charcoal-broiled steaks (as much as 8 µg benzpyrene/kg steak), as well as additives such as safrole, and pesticides such as Aramite and Dieldrin. Naturally-occurring carcinogens in various plants are also reviewed including cycads, cycasin, pyrrolizidine alkaloids, bracken fern, selenium, bacterial metabolites and mycotoxins. The epidemiology of cancer of the stomach and liver is related to dietary habits of various populations.

70-1015 A SPECIAL ROLE OF THE GROUP 17,18 CHROMOSOMES IN RETICULOENDOTHELIAL NEOPLASIA. (E.) Spiers, A. S. D. (Hammersmith Hosp. Leukemia Ther. Unit, London) and A. G. Baikie. Brit. J. Cancer 24(1):77-91, 1970. (60 references)

The variety of aberrations of group 17,18 chromosomes exceeds that of any other chromosome or group. Permutations of this group are discussed in relation to associated reticulo-endothelial neoplasms, including long-arm isochromosomes, monosomy, short-arm deletions, Ep- chromosome and a normal 17,18 complement. Ep- chromosome with 3 normal 17,18 group chromosomes, gain of a chromosome, long-arm deletion, Eq- and 4 normal 17,18 chromosomes, Eq and 3 normal group chromosomes, loss of a group chromosome and presence of an acrocentric chromosome, loss of 2 chromosomes and presence of 2 acrocentrics and a large short-arm member in the 17,18 chromosomes.

70-1016 EPIDEMIOLOGIC PATHOLOGY OF LEUKEMIAS AND LYMPHOMAS OF MAN. (E.) Lingeman, C. H. (NCI, Bethesda, Md.). Nat. Cancer Inst. Monogr. 32:177-209, 1969. (124 references)

The etiology, pathogenesis and epidemiology of various leukemias are discussed, including acute leukemias, chronic granulocytic leukemia, granulocytic sarcoma, chronic lymphocytic leukemia, childhood and neonatal leukemia. Lymphomas arising in various organs and tissues, Hodgkin's disease, Burkitt's tumor and disorders of the immune-protective system are similarly reviewed.

- 70-1017 TOXIC AND CARCINOGENIC ALKYLATING AGENTS FROM CYCADS. (E.) Spatz, M. (NIH, Bethesda, Md.). Ann. NY Acad. Sci. 163(2):848-859, 1969. (52 references)

The prenatal and postnatal effects of cycasin (β -D-glucosyloxymethane; a naturally-occurring glucoside used as a source of food by man in certain parts of the world) and its aglycone, methylazoxymethanol (MAM), are discussed. Cycasin is converted to its active product (MAM), either by the intestinal flora or by glucosidase activity in the skin. MAM was identified as a small molecule having hepatotoxic, neurotoxic, teratogenic, carcinogenic, mutagenic, alkylating and radiomimetic properties.

- 70-1018 THE HEALTH OF THE PUBLIC AND ASBESTOS USAGE. (E.) Royall, H. J. Roy. Inst. Pub. Health Hyg. J. 31(4-6):126-146, 1968. (49 references)

The types and nature of asbestos, its manufacture and the history of its usage, as well as its usage today, are discussed in relation to pulmonary fibrosis and mesotheliomas. Several series of case studies are reviewed of domestic and occupational exposure to asbestos in London and South Africa, and the pathology and histology of mesotheliomas are described.

- 70-1019 Science and Cancer. Shimkin, M. B. Public Health Service Publication No. 1162. U. S. Dept. Health, Education, Welfare, Washington, 1969, 159 pp, \$1.25.

- 70-1020 COCARCINOGENESIS. (Rus.) Turusov, V. S. (Acad. Med. Sci., Inst. Exp. Clin. Oncol., Moscow). Vop. Oncol. 15(6): 108-115, 1969.

- 70-1021 CURRENT PROBLEMS OF CHEMICAL CARCINOGENESIS. (Pol.) Górski, T. (Inst. Tumor Biol., Gliwice, Poland). Postepy. Hig. Med. Dosw. 23(5):569-600, 1969. (254 references)

- 70-1022 Survey of Compounds Which Have Been Tested for Carcinogenic Activity, Supplement 2. Shubik, P. and J. L. Hartwell (NCI, Bethesda, Md.). Peters, J. A. (Ed.) Public Health Service Publication No. 149, U. S. Govmt. Printing Office, 1969, 655 pp., 7.25.

- 70-1023 Carcinogenicity Testing. A Report of the Panel on Carcinogenicity of the Cancer Research Commission of the UICC. UICC Technical Report Series, Vol. 2. Berenblum, I. (Ed.) International Union Against Cancer, Geneva, 1969, 56 pp, \$2.00.

- 70-1024 SMOKING, LUNG CANCER AND RADIOACTIVE POLONIUM. (Dut.) Zijlstra, U. L. J. (U. Amsterdam). I. Soc. Geneesk. 47(23):775-779, 1969. (12 references)

- 70-1025 VIRUSES, AUTOIMMUNE DISEASE, AND CANCER. (E.) Leader, R. W. (Rockefeller U., Lab. Comp. Pathol., New York, N. Y.). Arch. Environ. Health (Chicago) 19(6): 824-826, 1969.

- 70-1026 LANGDON-DOWN DISEASE AND ACUTE LEUKEMIA. (Ger.) Mieler, W. (Ernst Moritz Arndt U. Pediat Clin., Greifswald, Germany). Paediat. Grenzgeb. 8(4):273-277, 1970. (15 references)

See also abstract no.: 1044

70-1027 BONE TUMORS AMONG THE ATOMIC BOMB SURVIVORS OF HIROSHIMA AND NAGASAKI.

(E.) Yamamoto, T. (Atomic Bomb Casualty Comm., Hiroshima, Japan) and T. Wakabayashi. Acta Path. Jap. 19(2):201-212, 1969.

Between 1950 and 1965, 163 bone tumors (30 autopsy, 133 surgical specimens) were found among the population of Hiroshima and Nagasaki. Only 25 malignant tumors were from persons exposed to the atomic bombs. Of the 76 malignant tumors, 70% were multiple myelomas and osteosarcomas; of the 87 benign tumors, 70% were osteochondromas and enchondromas. Among the pts. with osteosarcoma, 21 (81%) were younger than 39 yr. and 19 (73%) were male; 24 (92%) of the myeloma pts. were older than 40 and 15 (58%) were female. A fixed population sample of exposed and non-exposed persons from the 2 cities (about 12% of the total population) included only 24/163 bone neoplasms (15%). Exposure distance was not related to tumor frequency or type. No significant association between atomic radiation exposure and bone tumors, and no statistically significant differences in bone tumor frequency between exposed and non-exposed persons, were found.

70-1028 OSTEOSARCOMAS, FIBROSARCOMAS AND BASAL-CELL CARCINOMAS IN RABBITS AFTER IRRADIATION WITH GAMMA-RAYS OR FISSION NEUTRONS: AN INTERIM REPORT ON INCIDENCE, SITE OF TUMOURS AND RBE. (E.) Hulse, E. V. (Med. Res. Council, Didcot, Berkshire, England). Int. J. Radiat. Biol. 16(1):27-30, 1969.

Male and female rabbits (7-18-mo.-old) were irradiated in a natural uranium reactor. The incidence of osteosarcomas, fibrosarcomas (of the s.c. tissue) and basal cell carcinomas (of the skin) after at least 1 yr. were, resp., according to dose and type of irradiation: for γ -rays, (500 R, 4 animals) = 0, 0, 0; (1000-1300 R, 12 animals) = 1, 0, 4; (1400-1600 R, 5 rabbits) = 3, 1, 0; for neutrons (200 rads, 9 rabbits) = 0, 0, 0; (400-450 rads, 11 animals) = 2, 4, 1; (500-600 rads, 5 rabbits) = 2, 1, 0. The relative biological effectiveness of neutrons compared to γ -rays appeared to be of the order of 3. No tumors developed in the unirradiated rabbits.

70-1029 PAPILLARY CARCINOMA OF THE THYROID GLAND. SIZES OF 525 TUMORS FOUND AT AUTOPSY IN HIROSHIMA AND NAGASAKI. (E.) Sampson, R. J. (Atomic Bomb Casualty Comm., U.S. Marine Corps Air Station, Seattle, Wash.), C. R. Key, C. R. Buncher, H. Oka and S. Iijima. Cancer 25(6):1391-1393, 1970.

Autopsies at Hiroshima and Nagasaki showed papillary carcinomas of the thyroid in 251/1641 males and 274/1453 females. The logarithm of the greatest dimension of the tumor plotted

against the cumulative frequency showed a normal distribution for each sex, with the tumors in the females being consistently larger than tumors in males (mean sizes were 0.20 and 0.13 cm, resp.). Radiation was not a factor, as tumors in pts. receiving 50 or more rads were larger in females compared to those receiving a lower dose, and slightly smaller in males. The data suggested the presence of a growth-promoting factor, acting equally on radiation-initiated tumors and tumors initiated by other factors, which is greater in females than in males.

70-1030 ABERRATIONS IN LEUKOCYTE CHROMOSOMES OF PERSONNEL OCCUPATIONALLY EXPOSED TO LOW LEVELS OF RADIATION. (E.) Brown, J. K. (Australian Atomic Energy Comm. Res. Estab., Lucas Heights) and J. R. McNeill. Radiat. Res. 40(3):534-543, 1969.

Blood WBC from 10 male radiation workers (gamma group) who had received a lifetime dose of 7.7-36.0 rem (mostly γ rays) over 9-15 yr., and 10 males (neutron group) who received a lifetime dose of 0.4-13.1 rem γ rays and 0.3-4.4 rem fast neutrons over 4-12 yr., as well as 10 normal controls, were examined for chromosomal aberrations. Aneuploidy of the WBC was seen in 7-20% (av. 12.6%) of the controls, 7-24% (av. 13.6%) of the γ -exposed group, and 6-21% (av. 13.8%) of the neutron group. Acentric chromosomes were found in 3, 2 and 3 members of these groups, resp., and dicentric chromosomes in 1, 5 and 2 subjects, resp. The frequency of dicentrics was significant (probability about 0.02) in the γ -exposed group receiving 12.8-36 rem. No significant difference was seen between the total incidence of aberrations in the γ group (1.2%), the neutron group (0.8%) and the controls (0.9%).

70-1031 CHROMOSOME ABERRATION FOLLOWING RADIOPHOSPHORUS TREATMENT OF POLYCYTHAEMIA. (E.) Barnes, C. A. (U. Sydney Sch. Public Health Trop. Med., Australia), H. L. Holmes and P. L. T. Ilbery. Aust. Radiol. 13(4):396-417, 1969.

Chromosomes of peripheral blood and bone marrow cells from 51 pts. with polycythemia, treated by venesection (13 pts.), ^{32}P (33 pts.) or with busulfan (Myleran; 5 pts.) were examined. Total doses ranged from 3.2-32.5 mC; individual doses from 2.5-9.5 mC; and the interval between the first and last dose from 3 hr.-13.8 yr. Chromosomal aberrations were classified according to a system described by Buckton et al. There was a wide variation in all types of cytogenetic damage during the first 2 mo. after admin. of ^{32}P , but later, a definite increase in breaks and possibly all rearrangements was observed. The Cu-type damage (unstable; dicentrics,

tracentrics, and rings, with and without acentric fragments) was the most reliable indication of absorbed dose. B-type damage was retained in lymphopoietic stem cells for periods longer than 20 half-lives of ^{32}P . Similar changes were seen in cells from pts. treated with busulfan. In the only case of acute leukemia developing after ^{32}P therapy (28.5 mC), 2 clearly defined hypomodal clones were seen, with the absence of 1 or 2 group C chromosomes.

70-1032 BIOLOGICAL ACTIVITY OF RADIOACTIVE PHOSPHORUS, ^{32}P , IN THE MOUSE. (Sp.) Holmberg, E. A. D. (Nat. Acad. Med. Inst. Hemat. Res., Buenos Aires, Argentina), C. D. Pasqualini and S. L. Rabasa. Medicina (B. Air.) 28(Suppl. 1): 52-160, 1968.

Admin. of ^{32}P (i.p. in the form of Na_2PO_4) to BALB mice increased the incidence of leukemia significantly only in females. Castration during the first mo. of postnatal life increased the incidence of leukemia significantly in the male offspring of treated females, and in both male and female controls. Inoc. (i.p.) of cells of the ^{32}P -induced leukemia into mice of the same strain proved fatal within 8-20 days. These cells had a very short, marker chromosome and a modal number of 42. The i.p. inoc. of cell-free supernatants of leukemic organ homogenates into neonatal or 1-mo.-old mice induced leukemia in 1% and 53%, resp. An initial latent period of 3 mo. was reduced to 35 days by the passage 20 *in vivo*, with the number of takes in each passage ranging from 100-8%. Electron microscopic study confirmed the presence of A and C particles in the cells of leukemic organs, with the relative proportion of C particles increasing directly as the latent period decreased.

70-1033 ORIGIN OF NEOPLASTIC CELLS FOLLOWING PROPHYLAXIS OF RADIATION-INDUCED MOUSE LEUKAEMIA. (E.) Ilbery, P. L. T. (U. Sydney Sch. Public Health, Australia) and C. A. Barnes. Br. J. Cancer 5(1):124-135, 1970.

57 primary ^{60}Co radiation-induced leukemias in male mice, occurring after post-radiation cell complementation, over 90% abnormal classes and clones. The incidence of leukemia (approx. 70%) after the leukemogenic schedule of irradiation was lowered by grafts of bone marrow or fetal liver, but not abolished. Incidence of leukemia was also lowered by i.v. supplemented fetal thymus, but by no other lymphoid or thymic post-radiation treatment. All but 1 of the leukemias developed in irradiated cells. This is in contrast to the frequent occurrence of neoplasia in cell lines from non-irradiated thymic grafts after thymectomy and the same fractionated irradiation schedule. In 4/28 (C57BL x CBA.T6T6)F₁ leukemias, abnormal chromosomes undistinguishable from the marker were seen drawing attention, together with presumed loss of the marker in

another leukemia, to the frequency of non disjunction for this chromosome.

70-1034 DEVELOPMENT OF A MYELOPROLIFERATIVE DISORDER IN BEAGLES CONTINUOUSLY EXPOSED TO ^{90}Sr . (E.) Dungworth, D. L. (U. California, Davis), M. Goldman, J. W. Switzer and D. H. McKelvie. Blood 34(5):610-632, 1969.

Dietary ^{90}Sr (0.03-12 $\mu\text{C/day}$) was admin. to beagles from mid-gestation to 1.5 yr. of age. Myeloproliferative disorders were seen in 4 dogs given 4 $\mu\text{C/day}$ and in 10 given 12 $\mu\text{C/day}$, starting as early as 1 yr. of age and increasing in incidence. A continuous morphological spectrum was seen, ranging from an acute course (resembling granulocytic leukemia) to a chronic course (similar to myelofibrosis and myeloid metaplasia). The affected dogs showed a drop in hematocrit, with abnormal RBC morphology and a wide fluctuation of the WBC count (varying terminally from 3300 to 38,900). Most of the dogs (10/14) had splenomegaly (2-10 x normal wt.) and examination of the bone marrow showed extensive granulocytic proliferation with depletion of the erythroid and megakaryocytic indices. Histology of the spleen, liver, lymph nodes, lungs and kidneys of affected animals is described.

70-1035 TRYPSIN ESTERASE BINDING AND ITS RELATION TO THE RADIATION-LEUKEMIA PROTECTION (RLP) FACTOR. (E.) Yip, L. C. (Indiana U. Med. Ctr. Cancer Res., Indianapolis) and M. E. Hodes. Proc. Soc. Exp. Biol. Med. 133(4):1285-1288, 1970.

Trypsin-esterase binding activity (TEBA) and trypsin inhibiting capacity (TIC) of sheep serum and spleen extracts were studied. TEBA activity followed the radiation-leukemia protection (RLP) elution pattern for spleen, but not for serum. TEBA of serum and spleen differed in stability to heat and pH changes. Activity of spleen was more sensitive to heating at 60°; under dialyzing conditions, serum activity was stable at pH 4.5, but spleen TEBA was almost inactive. At pH 9.5, both spleen and serum retained 65-72% of their activity. TIC of sheep serum was present in most Sephadex G-200 fractions, but that of spleen was confined to 19S material and also corresponded to the TEBA of that peak. After exposure of mice to 300 R, TEBA of their serum decreased and remained depressed for several days; inj. of sheep serum, but not saline or albumin, restored the TEBA; similar results were obtained with C57BL/6 and Swiss mice. It is thought that RLP may exist as a complex with α_2 -macroglobulin.

70-1036 COMPARATIVE CYTOMORPHOLOGY OF IRRADIATION ATYPIA AND CHEMICALLY INDUCED CARCINOMA IN THE MOUSE CERVIX. (E.) Burdman, D. (Long Island Jewish Hosp.-Queen's

Hosp. Ctr. Affil., Jamaica, N. Y.), M. Garret and D. L. Benninghoff. *Acta Cytol.* (Balt.) 13(11):620-633, 1969.

The cervixes of 8-week-old C3H mice (81 animals) were subjected to 2000-3000 r of X-irradiation, painting with a 1% soln. of benzpyrene, or both. Irradiation of the normal cervix produced atypical benign cells, mostly of a squamous metaplastic type which had pyknotic nuclei similar to malignant cells, and a pseudoanaplastic type with vesicular nuclei, similar to the malignant cells. Only the well-preserved, mononucleated anaplastic cells were not simulated by the irradiated benign cells. Malignant cells which were irradiated showed typical radiation changes and over-all enlargement when compared to unirradiated malignant cells which, in turn, had a more greatly increased nuclear size, nucleocytoplasmic ratio, and hyperchromasia than irradiated benign cells.

70-1037 SQUAMOUS CARCINOMA OF THE BODY OF THE UTERUS. (E.) Hopkin, I. D., R. A. Harlow and P. J. Stevens (Queen Victoria Hosp., East Grinstead, Sussex, England). *Brit. J. Cancer* 24(1):71-76, 1970.

A well-differentiated squamous cell carcinoma of the corpus uteri was found in an 83-yr.-old woman, who had had 2 children (at the ages of 34 and 38 yr.) and a radium-induced menopause for menorrhagia at the age of 48 yr. No carcinoma of the cervix, no endometrial adenocarcinoma and no connections between the tumor and the squamous epithelium of the cervix uteri, were found in the surgical specimen. The pt. had no history of pyometra. The significance of the radiation-induced menopause (35 yr. before the diagnosis of cancer) is discussed, but no conclusions could be drawn.

70-1038 AN EVALUATION BY ALPHA-PARTICLE BRAGG PEAK RADIATION OF THE CRITICAL DEPTH IN THE RAT SKIN FOR TUMOR INDUCTION. (E.) Heimbach, R. D. (New York U. Med. Ctr., N. Y.), F. J. Burns and R. E. Albert. *Radiat. Res.* 39(2):332-344, 1969.

The dorsal skin of male albino CD rats (58-59-days-old) was irradiated with 37-million-electron-volt α particles in a linear depth-dose pattern (penetrating 1.09 mm) or in a Bragg peak dose (at depths of 0.12, 0.35, or 0.55 mm). The tumor incidence with a surface dose of 1050 rads (linear) was 1.68/rat; in those receiving Bragg peak irradiation at a surface dose of 2460 rads, the incidence was 0, 1.01 and 0.59 tumors/rat, resp. The incidence of abnormal hair follicles was analogous to that of tumors with a ratio of 9000:1 (abnormal follicles to tumors). As the follicle depth is about 0.3 mm, the results indicated that follicle injury and tumor incidence depend on the radiation to the

entire follicle and the capacity for repair depends on the part of the follicle minimally damaged.

70-1039 HISTOPATHOLOGY OF PRIMARY LUNG TUMOURS IN THE MOUSE. (E.) Amaral-Mendes, J. J. (Nat. Lab. Vet. Res., Lisbon). *J. Path.* 97(3):415-427, 1969.

Primary lung tumors were examined, from SAS/4 albino mice that had received single whole-body irradiation in air and under hypoxic conditions (352 tumors including controls), or that had received ionizing radiation and either urethan (2 mg/g) or 7,12-dimethylbenzanthracene (2.0 μ g/g; 743 tumors including controls). A sample group of 67 mice was chosen; 105 tumors in these mice were classified as Type A (alveolar) and 106 tumors were classed as Type B (bronchiolar). Cells of Type A were more variable in size, had a nucleus:cytoplasm ratio of less than 1, had an acidophilic and granular cytoplasm, were periodic acid-Schiff (PAS)-negative and more pleomorphic, and showed fewer mitotic figures. Type B cells were larger, with a nucleus:cytoplasm ratio of greater than 1, had a basophilic cytoplasm, and were PAS-positive with many mitotic figures. An intermediate type (112 tumors) was also noted. Chronic collapse, especially collapsed areas infiltrated with leukemic cells of the lymphocytic type, and inflammatory changes were associated with pulmonary tumors.

70-1040 EFFECT OF INTERFERON ON THE COURSE OF SPONTANEOUS AND RADIATION-INDUCED RENAL LESIONS IN THE RF/Un MOUSE. (E.) Guttman, P. H., W. C. Davis, H. H. Fudenberg (U. California Med. Ctr., San Francisco) and T. C. Merigan. *Vox. Sang.* 17(4):279-288, 1969.

RF/Un mice were X-irradiated at birth (single whole-body dose of 425 R); irradiated and non-irradiated mice were inj. i.p. with 0.2 ml of interferon (prepared from L cells infected with Newcastle disease virus) or spent culture medium, and sacrificed at 70-80 days of age. All survivors (117/274) had characteristic intercapillary glomerulosclerosis; the glomeruli in the outer cortex were most severely affected. The most severe lesions were seen in 10/21 irradiated mice inj. with spent culture medium, compared to 1/20 non-irradiated mice inoc. with interferon and 7/17 mice treated with irradiation only. In animals treated with interferon (both irradiated and non-irradiated), the frequency of severe lesions was reduced. The light and electron microscopic appearance of lesions was described. The occurrence of the kidney lesions was independent of the incidence of myeloid leukemia, suggesting that if this glomerulosclerosis is mediated by a virus, the virus is different from the agent responsible for the high incidence of myeloid leukemia in mice of this strain.

70-1041 INFLUENCE OF ENVIRONMENTAL LIGHT AND MELATONIN UPON MAMMARY TUMOUR INDUCTION. (E.) Hamilton, T. (U. Edinburgh Med. Sch.). Brit. J. Surg. 56(10):764-766, 1969.

Female Sprague-Dawley rats were exposed to 12 hours of light and 12 hours of darkness, or to 24 hours of constant illumination. Each morning, 100 µg melatonin was inj. s.c. into some rats; after 1 week, all rats received 9,10-dimethylbenzanthracene (30 mg by gastric intubation). In diurnal light, after 8 mo., 15/26 rats developed mammary tumors (20 fibroadenomas and 6 carcinomas); in constant light, 20/21 developed mammary tumors (53/57 were fibroadenomas). The ovaries and pineal glands in rats exposed to constant light were reduced in wt., the pituitaries were increased in wt. and no change was seen in adrenal, uterine or body wt. The only significant change with melatonin was seen under diurnal light conditions; 6/8 controls developed mammary tumors compared to 7/7 treated rats, with 14/21 fibroadenomas in the former group and 26/32 carcinomas in the latter.

70-1042 BREAST CANCER FOLLOWING MULTIPLE FLUOROSCOPIES DURING ARTIFICIAL PNEUMOTHORAX TREATMENT OF PULMONARY TUBERCULOSIS. (E.) Myrden, J. A. (5880 Spring Garden Road, Halifax, Nova Scotia) and J. E. Hiltz. Canad. Med. Ass. J. 100(22):1032-1034, 1969.

A 43-yr.-old woman, with a breast tumor which developed 14 yr. after receiving over 200 fluoroscopic examinations in the course of artificial pneumothorax treatment for pulmonary tuberculosis (TB), is described. A follow-up study was made in 1966 of 1581 pts. treated for TB at the Nova Scotia Sanatorium from 1940-1949. Breast cancer developed in 22/483 women (7.3%) treated by artificial pneumothorax with fluoroscopy, and in only 4/483 (0.83%) of those women receiving other treatment. None of the 920 treated males developed breast cancer. All those who developed breast cancer in the pneumothorax group began treatment when less than 29 yr. old. The av. time of development from the beginning of treatment was 17 yr. and the av. age was 39. Of 10 cancer pts. who received treatment for the left lung, 8 developed cancer of the left breast; similarly, 6/7 treated by pneumothorax for the right lung had cancer of the right breast, and 1/5 who had received bilateral pneumothorax, developed bilateral breast cancer. All but 3 pts. had received more than 75 fluoroscopic examinations and 13 of the cancers (60%) developed in pts. who had received more than 175 fluoroscopies each.

70-1043 ON SOME PECULIAR PATHOLOGICAL FEATURES OF LUNG SCAR CANCER. (E.) Bajtai, A.

(Postgrad. Med. Sch., Budapest) and J. Juhasz. Arch. Ital. Pat. Clin. Tumori 12(1-2):95-108, 1969.

Between 1957 and 1967, 74 (21.5%) lung scar cancers were seen among 344 pts. with primary lung cancer. The neoplasms were located mostly in the upper lobes and were of the alveolar or squamous cell type. The av. age of the 74 pts. was 60.2 yr.; the male:female ratio, 3.35:1. The pleura over the involved areas was described as hyalinized, thickened and depressed, and differentiated from bronchogenic carcinoma by a central tumor-free scar with elastosis and occluded arteries. There was evidence of malignant transformation of both the alveolar and bronchial epithelium; etiologically, 31/74 cases had prior histories of tuberculosis.

70-1044 EARLY DEMONSTRATION OF DORMANT OR NON-DORMANT, MICROSCOPIC BRONCHOPULMONARY CANCERS BY EXFOLIATIVE CYTOLOGY. (Fr.) Brun, J. (St. Eugénie Hosp., Lyon-Saint-Genis-Laval, France), J. Kofman and F. Magnin. Poumon Coeur 25(2):113-127, 1969.

A review (26 references) of the development and detection of incipient, microscopic foci of malignancy at the site of sclerotic areas of chronic irritation in the bronchopulmonary tract or at the site of tubercular or other bronchogenic and pulmonary lesions (frequently first signalized by the presence of malignant cells in the sputum in the absence of X-ray, bronchoscopic or other indications of actual tumefaction), is supplemented by 5 illustrative case histories. These appear to confirm that such foci of malignant proliferation in the presence of non-malignant disorders may or may not be subject to further, pejorative evolution, with a relatively long period of latency or "dormancy" frequently intervening before an actual tumor starts to develop.

70-1045 CARCINOMA OF THE OESOPHAGUS AFTER GASTRIC SURGERY. (E.) Shearman, D. J. C. (U. Edinburgh Roy. Infirm.), S. J. Arnott, N. D. C. Finlayson and J. G. Pearson. Lancet 1(7647):581-582, 1970.

Of 92 pts. with esophageal squamous cell carcinoma, 8 (6 males, 2 females, age 52-74 yr.) had previously undergone partial gastrectomy or gastroenterostomy over periods of 6-40 yr. (av. 19 yr.) previously; 6/8 tumors occurred in the lower esophagus. Only 1 pt. had received previous radiotherapy; 1 pt. had a low serum vitamin B₁₂ level, and 6 pts. had a low serum iron level. The incidence of this association with gastric surgery (9%) was greater than any other known association, such as achalasia.

See also abstract nos.: 1024, 1046, 1081, 1342, 1343, 1381, 1392, 1399, 1404, 1405

70-1046 FURTHER STUDIES ON SERUM PROTEIN FORMATION BY CHIMERAS: INDUCTION OF CHIMERISM WITH A CHEMICAL CARCINOGEN. (E.) Kikuchi, Y. (Hokkaido U. Sch. Med., Sapporo, Japan) and M. E. Phillips. Cancer Res. 30(1): 18-23, 1970.

Bone marrow cells from 200-250 g Sprague-Dawley rats were inj. i.v. into 56, 25-40 g C57BL/6 male mice, 1-2 weeks after treatment with 5 or 10 mg 3-methylcholanthrene (MC) alone or with 450 roentgens of whole-body X-irradiation. Animals receiving MC alone and marrow cells after 1 week seemed to have a longer survival time than mice receiving marrow cells after 2 weeks. Mice were sacrificed weekly and the spleens and mesenteric lymph nodes cultured for 24-48 hr. Synthesis of rat immunoglobulin G₂ was seen as early as 1 week after marrow transplant, in the culture fluid of spleen and nodes of chimeras treated with 5 mg MC and no irradiation, and with less intensity in the irradiated mice. Mice receiving 10 mg MC did not survive longer than 3 weeks, but demonstrated some rat immunoglobulin synthesis at that time. Splenic tissues from chimeras synthesized mouse immunoglobulins in all groups at 2-3 weeks after marrow transplants.

70-1047 HORMONALLY ACTIVE OVARIAN TUMORS IN RABBITS INDUCED BY METHYLCHOLANTHRENE. (Pol.) Rózewicki, S. (Med. Acad. Inst. Anat. Path., Stettin, Poland) and B. Pohnke. Pat. Pol. Suppl. 1:153-154, 1969.

Surgical introduction of 20 mg of 3-methylcholanthrene into the right ovaries of 35 randomly selected 6-9-mo.-old female rabbits resulted after 2 yr. in the development of hormonally active tumors (luteomas and thecomas - no other detail) in 8 animals. The left ovaries and 27 right ovaries without tumors did not differ from normal ovaries and contained a variable number of primary follicles in the cortical layer. The cortex of the right, unaffected ovaries showed empty spaces of different size (from methylcholanthrene) surrounded by non-specific granulation tissue.

70-1048 PRODUCTION OF EXPERIMENTAL BRAIN TUMOURS BY 20-METHYLCHOLANTHRENE IN SWISS MICE. (E.) Sil, R. (Inst. Postgrad. Med. Ed. Res., Calcutta, India). Neurol. India 18(4):203-206, 1969.

Inbred Swiss mice (8-10 weeks old) were inj. intracranially under anesthesia with 1.5 mg 3-methylcholanthrene. Of the 35 mice treated, 25 survived to the end of the observation period (about 180 days); 3 died before the appearance of tumor and 4 died suddenly after the appearance of tumor due to edema of the brain. Histological examination showed 18/25 highly cellular

sarcomatous tumors with hyperchromatic nuclei, 4 were spongioblastomas and 3 were unclassifiable gliomas.

70-1049 QUALITATIVE AND QUANTITATIVE STUDIES ON THE METABOLISM OF A SERIES OF AROMATIC HYDROCARBONS BY RAT-LIVER PREPARATIONS. (E.) Sims, P. (Chester Beatty Res. Inst. Roy. Cancer Hosp., London). Biochem. Pharmacol. 19(3): 795-818, 1970.

Liver microsomes, from male Chester Beatty rats inj. i.p. with 5 mg 3-methylcholanthrene in arachis oil, were analyzed for their metabolism of tritium-labeled benzantracene, dibenz(a,h)anthracene, dibenz(a,c)anthracene, benzo(a)pyrene, benzo(e)pyrene, 3-methylcholanthrene, 7-methylbenzantracene, 7,12-dimethylbenzantracene, phenanthrene, pyrene and chrysene. Qualitatively, all the major ethyl acetate-soluble metabolic products were accounted for and probable structures given. Quantitatively, the amounts of metabolites were increased in the microsomes of methylcholanthrene-treated rats, but the amounts of dihydrodiols formed on the "K region" varied with each hydrocarbon.

70-1050 IRREVERSIBLE METHYLCHOLANTHRENE-INDUCED THYROIDITIS IN BUFFALO STRAIN RATS. (E.) Reuber, M. D. (NCI, Bethesda, Md.) and E. L. Glover. Path. Microbiol. (Basel) 34(1): 60-64, 1969.

Inbred 12-week-old female Buffalo rats (about 188 g) were fed a diet containing 0.033% 3-methylcholanthrene (MC) for 12 weeks and either sacrificed or put on a normal diet. After being continued for 12 weeks on a normal diet, the av. body wt. was about 18 g less than in controls. After 24 weeks, all rats were ill; 4 died with acute necrotizing bronchopneumonia and an av. wt. loss of 64 g. Thyroiditis was seen in 7/13 rats sacrificed after 12 weeks of feeding with MC, in 9/13 continued on a normal diet for 12 weeks, and in 11/14 after 24 weeks on a normal diet, but severe thyroiditis was more frequent in the first group than in the others.

70-1051 SOME OBSERVATIONS ON THE MORPHOLOGY AND HISTOCHEMISTRY OF EXPERIMENTAL BRAIN SARCOMAS IN MICE. (E.) Kroh, H. (Pol. Acad. Sci. Exp. Clin. Med. Res. Ctr., Warsaw). Folia Histochem. Cytochem. (Krakow) 7(1):47-58, 1969.

Experimental brain sarcomas, induced in C3H and RIII mice after implantation with 3-methylcholanthrene, were divided into 4 groups: Group I - fibrosarcomas of the dura mater (7), containing low alkaline phosphatase (ALP) and significant non-specific esterase in the

cytoplasm with low levels of AIP in the blood vessels; Group II - endothelial meningiosarcomas (2), containing low levels of AIP in the vessels and high non-specific esterase in the fusiform cells; Group III - osteosarcomas (3), containing high AIP in the cytoplasm and low activity in the vessels and a high non-specific esterase activity in 30% of the neoplastic cells; and Group IV - circumscribed sarcomas of the blood vessels (7), containing no AIP activity in the endothelium of the blood vessels. The activity of acid phosphatase and aminopeptidase was not distinctive in any of the sarcomas. The histology of each was described.

70-1052 EXPERIMENTAL CARCINOMA AND ENDOCRINE BACKGROUND. REPORT I. INDUCTION, TRANSPLANTATION AND CANNULATION TECHNIQUES OF PROSTATIC CARCINOMA INDUCED BY 20-METHYLCHOLANTHRENE AND HYPOPHYSEAL ADRENAL HORMONE REGULATIONS. (E.) Hirai, M. (Jikei U. Sch. Med., Japan), S. Shima, Y. Urata, Y. Masubuchi and T. Nakao. Jikeikai Med. J. 16(3-4):91-103, 1969.

At least 1 mg of 3-methylcholanthrene was applied by a silk thread to the ventral prostate of 8- or 9-week-old, 150-180 g male Donryu rats. After 20 weeks, 21/93 had squamous cell carcinoma of the prostate, which was transplanted s.c. to male and female rats of the same strain. Treatment of young male rats bearing the transplanted tumor with 5 I.U. of ACTH or 1 mg corticosterone s.c. for 10 days inhibited tumor growth, while hypophysectomy or adrenalectomy of young adult male rats also caused inhibition of their transplanted tumor. Measurement of the adrenal corticosterone conc. at 8 and 16 days after tumor implantation indicated a decrease with time, but there was no significant difference from the controls in each group. ACTH (10 I.U.), given 5 days after adrenalectomy, seemed to induce a corticosterone-like substance in tumor-bearing rats.

70-1053 CYTOLOGICAL STUDY OF INDUCED TUMOURS IN RAT. (E.) Talukder, G. (Univ. Coll. Sci. Cytogenet. Lab., Calcutta, India) and A. K. Sharma. Indian J. Cancer 6(2):93-98, 1969.

Inbred albino rats, 18 males and 18 females, were inj. in the abdominal wall (2 inj./week for 4 weeks) with 0.25 ml 0.5% 3-methylcholanthrene (MC) or 0.5 ml 0.2% 3,4-benzpyrene (BP). The induced solid tumors and 2 ascites tumors (1 spontaneous and 1 from the MC group), were prepared for chromosomal studies. The modal chromosome number in a majority of cells in the BP-induced tumors was 60-74, compared to 50-64 in the BP-induced tumors and 66-78 in 70% of the cells from the MC-induced ascites tumor. Structural variations, like those seen in human tumors, mostly involved the shorter chromosomes.

70-1054 MICROSPECTROPHOTOMETRIC STUDIES OF DNA ON THE EPITHELIAL TUMORS INDUCED BY 3-METHYLCHOLANTHRENE AND CROTON OIL TREATMENT IN MICE. (E.) Manocha, S. L. (Emory U. Yerkes Reg. Primate Res. Ctr., Atlanta, Ga.). Acta Histochem. (Jena) 34(2):201-211, 1969.

A 0.05% soln. of 3-methylcholanthrene was painted on the shaved backs of male and female Swiss mice (28-38 g; 2-3 mo.-old) at weekly intervals for 6 weeks, followed, after 2 days, by 1.0% croton oil continued for 40 weeks. Although croton oil alone had no tumorigenicity, greater than 50% of the induced papillomas regressed after it was discontinued. A lower incidence of tumors in female mice was thought to be due to less physical trauma. Chromosomal abnormalities (fragments and bridges) showed a high correlation with the stage of growth of the tumor; also, as tumor growth progressed, the diploid DNA content underwent tetraploid and aneuploid transformation.

70-1055 ROLE OF BOVINE GROWTH HORMONE IN CHEMICALLY INDUCED SKIN CARCINOGENESIS IN SWISS ALBINO MICE. (E.) Tipnis, U. V. (Tata Mem. Ctr. Cancer Res. Inst., Bombay, India) and S. M. Sirsat. Indian J. Exp. Biol. 7(4):197-201, 1969.

Squamous cell carcinomas were induced in weanling Swiss albino mice, 20-23 weeks after painting the abdominal skin with 0.25% 3-methylcholanthrene (MC; 2 paintings/week); tumors were observed after 16-24 weeks in mice painted with MC and inj. with saline (also 2 doses/week), upon appearance of papillomas. When bovine growth hormone (BGH) was inj. s.c. (0.2 mg in 0.2 ml of saline) along with biweekly treatment of carcinogen, starting on the appearance of papillomas, tumors were observed in 16-24 weeks; and when BGH (0.4 mg) was given prior to, then alternated with, MC, tumors were induced in 12-20 weeks. Tumor growth was restricted to the upper dermis in mice receiving MC or MC + saline, while those receiving hormone and MC showed marked dermal edema and deep and lateral invasion of the dermis.

70-1056 EVALUATION OF THE RESPONSE OF Bufo arenarum LARVAE TO 20-METHYLCHOLANTHRENE. (E.) Matos, E. L. (U. Buenos Aires Roffo Inst. Oncol., Argentina) and E. S. de Lustig. Oncology 24(1):68-78, 1970.

Bufo arenarum larvae were inj. s.c. with 0.02 ml of a 0.25% soln. of 3-methylcholanthrene suspended in olive oil. Within the first 3 days, 20% of the epidermal specimens showed epithelial hyperplasia with cellular disorientation, anisocytosis and an increased mitotic activity localized to the site of inoc. The single

epidermal cell layer was increased to almost 9 layers; after a few more days, adenomatous foci were observed. An inflammatory process was present in both experimental animals and those inj. only with olive oil. From 9-20 days, a papillomatous formation or epithelial invasion was seen beneath the basal membrane, sometimes with pseudotumoral nodular formations. After 20 days, this process underwent regression.

70-1057 THE PROBLEM OF CARCINOGENESIS (TRANSFORMATION OF NORMAL INTO MALIGNANT CELLS). (Ger.) Bianchi, L. (U. Basel Path. Inst., Switzerland) and W. Oehlert. Praxis 58(24):759-764, 1969.

Cell kinetics during carcinogenesis of mouse skin after application of 3-methylcholanthrene were studied using ^3H -thymidine histoautoradiography. It was shown that physiological cell loss in normal skin is compensated by the unequal cell division (resulting in an intermitotic and postmitotic cell) taking place in the basal "indifferent zone". The same holds true for regeneration after superficial skin lesions. The mitotic cycles of the cells of the basal membrane are subject to several different regulatory mechanisms. Application of carcinogen first causes hyperplasia, then benign skin papilloma (after 50-60 days) and finally carcinoma (after a latency of 80-90 days). Hyperplasia and papilloma are characterized (as is regeneration) solely by an increased proliferation of cells of the "indifferent zone" whereby the unequal cell division is maintained. The appearance of the so-called "reticulation zone" in papillomas is the turning point in the transformation of normal into malignant cells. It is characterized by the disappearance of the "indifferent zone" and unequal cell division, loss of cell differentiation, and an increased cell proliferation. The cells of the "reticulation zone" are autonomous, not subject to regulatory mechanisms, and are the stem cells of carcinoma. It is concluded that the carcinogen causes an unexplained initial damage which is transmitted to daughter cells, is potentiated and, after a latency period, expresses itself in reticulation and carcinogenesis. It is also suggested that several cell generations are necessary for carcinogenesis to take place.

70-1058 POTENTIATING EFFECT OF THALIDOMIDE ON METHYLCHOLANTHRENE ONCOGENESIS IN MICE. (E.) Miura, M., C. M. Southam (Sloan-Kettering Inst. Cancer Res., New York, N. Y.), and H. Wuest. Experientia 26(3):305-306, 1970.

Thalidomide (TH; 25 mg for 5 days in each of 4 consecutive weeks; admin. i.p. or p.o.) was given to 4-mo.-old female Swiss mice; a 1% soln. of 3-methylcholanthrene (MC) in benzene was admin. to the skin for 5 consecutive days beginning 1 week after the initial dose of TH. In 1

experiment, this course was repeated for another 5 consecutive days after a 2-day interval. The massive doses of TH had no discernible toxicity. Mice admin. TH i.p. showed approx. twice the skin papilloma response to MC as did controls; mice given TH p.o. also had a slightly greater papilloma response. During i.p. TH treatment, the mean hemolysin response was 1:120 and the av. number of hemolytic plaques was 1050/million spleen cells, as compared with 1:480 and 1600, resp., for carboxymethyl cellulose-treated controls. Antibody production was not decreased in mice tested after TH treatment was stopped.

70-1059 RIBONUCLEIC ACID-MEDIATED INHIBITION AND ENHANCEMENT OF TUMOR GROWTH IN MICE. (E.) Ramming, K. P. (NCI, Bethesda, Md.) and Y. H. Pilch. Surg. Forum 20:106-109, 1969.

RNA was extracted from regional lymph nodes and spleens of Hartley guinea pigs 12 days after inj. of cells from a 3-methylcholanthrene-induced C57/Bl6 mouse sarcoma (MC-3) in the footpads with Freund's adjuvant and i.p. without, then incubated with normal C57 spleen cells. The spleen cells ($1-10 \times 10^8$) were inj. i.p. along with 10^3 MC-3 cells s.c. into normal C57 mice; treated spleen cells were admin. the next day. At day 21, 10/21 mice admin. treated spleen cells developed tumors, compared to 21/27 controls. Similar results were seen using benzpyrene-induced mouse sarcomas in C3Hf/HeN mice and C3H spleen cells. Inhibition of tumor development was also observed when the spleen cells were incubated with RNA from guinea pigs immunized with normal C3H tissues. Spleen cells incubated with RNA and treated with RNA-ase had no inhibitory effect, and tumor cells mixed with RNA-incubated spleen cells prior to inj. increased the tumor incidence.

70-1060 LIGAND INTERACTIONS WITH HEMOPROTEIN P-450. II. INFLUENCE OF PHENOBARBITAL AND METHYLCHOLANTHRENE INDUCTION PROCESSES ON P-450 SPECTRA. (E.) Jefcoate, C. R. E. (Cornell U., Ithaca, N. Y.) and J. L. Gaylor. Biochemistry (Wash.) 8(8):3464-3472, 1969.

Cytochrome P-450 (oxidized) in the submicrosomal particles from the liver of New Zealand rabbits, after pretreatment with 3-methylcholanthrene (MC), showed a new hemoprotein with spectral peaks of 395, 505 and 650 m μ . Electron paramagnetic resonance spectra of microsomes from rabbits treated with MC showed a new signal characteristic of iron in a high-spin state, in about equal quantities to the usual low-spin hemoprotein, which was also present. The proportion of ^{14}C -MC increased in the nonpolar component of the medium as the proportion of high-spin P-450 decreased, indicating the absence of direct binding of MC to P-450. A close similarity was observed between the electron paramagnetic spectra of metmyoglobin-n-

propylmercaptide and the low-spin form of P-450, and the affinities of certain organic ligands were reversed between metmyoglobin and P-450. Protein ligand binding of the 2 hemoproteins and P-450 is discussed.

- 70-1061 INDUCTION OF DRUG METABOLISM. III. FURTHER EVIDENCE FOR THE FORMATION OF A NEW P-450 HEMOPROTEIN AFTER TREATMENT OF RATS WITH 3-METHYLCHOLANTHRENE. (E.) Shoeman, D. W. (U. Minnesota, Minneapolis), M. D. Chaplin and G. J. Mannering. *Molec. Pharmacol.* 5(4):412-419, 1969.

Male Holtzman rats (80-90 and 180-200 g) were inj. i.p. with phenobarbital sodium (PB; 40 mg/kg/day) 3-methylcholanthrene (MC; 20 mg/kg/day) for 4 or 5 days and the liver microsomal hemoprotein examined. PB treatment produced microsomes that increased difference spectra with both hexobarbital (type I binding) and aniline (type II binding), but MC only increased the type II binding component while the type I component appeared to decrease. Treatment with 0.07% steapsin for 24 hr. at 0°C reduced hexobarbital binding of microsomes from untreated (73%), PB-treated (66%), and MC-treated (100%) rats. The cytochrome P-450 content decreased 46, 41, and 35% resp. Aniline binding was increased. Storage in the cold decreased both components, especially the type I.

- 70-1062 BIPHASIC DECREASE OF RADIOACTIVE HEMOPROTEIN FROM LIVER MICROSOMAL CO-BINDING PARTICLES. EFFECT OF 3-METHYLCHOLANTHRENE. (E.) Levin, W. (Burroughs Wellcome Co. Res. Labs., Tuckahoe, N. Y.) and R. Kuntzman. *J. Biol. Chem.* 244(13):3671-3676, 1969.

Long-Evans rats were inj. i.p. with 25 mg/kg/day 3-methylcholanthrene or corn oil for 3 days, and 24 hr. later, received 0.234 mg/kg i.v. of ³H-delta-aminolevulinic acid. Radioactivity was seen in the CO-binding particles (the microsomal hemoprotein with cytochrome b₅ removed by treatment with steapsin) 1 minute after inj. of the label, and reached a max. within 30-60 minutes. No difference in the incorporation of radioactivity was seen between the control and treated rats, but a biphasic disappearance of radioactivity from the CO-binding particles indicated the presence of 2 hemoprotein fractions. The ratio of the fast phase component to the slow component in the treated rats was 1:1 compared to 3.8:1 in the controls, mainly due to 3-4-fold increase in the content of slow phase hemoprotein in the treated rats.

- 70-1063 IMMUNOLOGIC STUDIES ON CARCINOGENESIS. (E.) Humphrey, L. J. (U. Kentucky, Lexington), P. Lincoln, L. Hunter and W. R. Jewell. *Current Topics Surg. Res.* 1:91-103, 1969.

Female C3H/HeHa mice were inj. s.c. with 0.25 mg methylcholanthrene (MC) and/or MC-induced sarcoma homogenate. Mouse 3T3 cell cultures were treated similarly *in vitro*. After 10 weeks, tumors developed in 5/36 mice inoc. with MC alone, 4/30 inj. with homogenate, and 21/35 inj. with both. Tumors in those treated with homogenate were round and discrete with a different cell type from the others. The treated cell cultures were incubated from 3-9 mo., and 1×10^6 cells were inj. s.c. into weanling mice, but no tumors developed. No precipitation line was seen when sera from mice bearing a MC-induced sarcoma or from mice bearing a MC-induced sarcoma was tested against a MC-induced sarcoma, spleen or kidney-liver suspension. However, sera from 4/6 giant Flemish rabbits, immunized with MC-induced sarcoma, developed a precipitation line when tested against the antigen.

- 70-1064 NEGATIVE RESULTS OF ATTEMPTS TO PROLONG THE EFFECT OF PHOSPHOLIPIDS (PL) AND CHOLESTEROL (Chol) ON THE FORMATION OF TUMOURS INDUCED BY 3-METHYLCHOLANTHRENE (MeC). (E.) Altman, R. F. A. (O Hosp., Rio de Janeiro, Brazil), D. J. Da Silva and C. R. N. Lopes. *Z. Naturforsch.* [B.] 25b(2):229-230, 1970.

Swiss mice were divided into 11 groups of 20, each receiving 3-methylcholanthrene (MC; 0.5 mg s.c. in 0.2 ml triolein). Additional phospholipids (PL) or cholesterol were given to 5 groups each at various dosage schedules and different routes of admin.; 1 group remained as a control. By week 12 after treatment with MC, 50% of the controls had developed tumors as compared to 15-36% of those given PL and 89-95% of those given cholesterol, except when the PL or cholesterol were admin. i.v. At week 16, all those receiving cholesterol had died from cancer, but tumor incidence in the group given PL was similar to that of the controls. The high mortality of the i.v.-inj. mice was attributed to lack of an adequate stabilizer in the emulsion.

- 70-1065 MALIGNANT TRANSFORMATION *IN VITRO* WITH CARCINOGENIC HYDROCARBONS. (E.) Heidelberg, C. (U. Wisconsin Med. Sch. McArdle Lab., Madison), T. T. Chen and P. T. Iype. *Advances Enzym. Regulat.* 7:339-349, 1969.

When normal C3H mouse ventral prostate (not showing spontaneous transformation) was cultivated *in vitro* and exposed to 3-methylcholanthrene (MC; 1 µg/ml), cell lines developed which were resistant to MC toxicity, grew into random piled-up colonies, and induced progressive transplantable tumors in adult C3H mice. This method is proposed as the basis for a quantitative, reproducible method of *in vitro* carcinogenesis by carcinogenic hydrocarbons.

70-1066 CHROMATIN BINDING OF BENZO(a)PYRENE
AND 20-METHYLCHOLANTHRENE. (E.)

O'Brien, R. L. (U. Southern California Sch. Med., Los Angeles), R. Stanton and R. L. Craig. *Biochim. Biophys. Acta* 186(2):414-417, 1969.

Liver chromatin-hydrocarbon complexes were formed *in vivo* by inj. of male Sprague-Dawley rats with ³H-labeled 3,4-benzpyrene (BP) or 3-methylcholanthrene (MC; 30-200 mg/kg; i.p.; dissolved in corn oil or dimethyl sulfoxide. The absorption spectrum of BP bound to chromatin *in vivo* was lower than that of BP bound to DNA *in vitro*; none was found for bound MC. The fluorescence spectrum of BP bound *in vivo* was at wavelengths 6-8 nm shorter than the peaks for BP bound to DNA; those for MC were identical. The shifts for BP suggested that it was bound to chromatin in a less polar local environment than when bound to DNA. The amount of hydrocarbon bound to chromatin *in vivo* was a function of time and of the amount of hydrocarbon admin.; the max. amount was bound to chromatin between 1 and 3 hours. It was concluded that the major portion of the hydrocarbons bind to chromatin proteins and not to DNA.

70-1067 STIMULATION OF DOPA-OXIDASE POSITIVE
MELANOCYTES DURING CARCINOGENESIS OF
THE SKIN. (Ger.) Rohrbach, R. (Univ. Path.
Inst., Freiburg i. Br., Germany). *Virchow.
Arch. [Zellpath.]* 3(2):219-228, 1969.

Hairless hr/hr mice treated with 3-methylcholanthrene or 7,12-dimethylbenzanthracene (2 drops of 0.5% soln. in acetone, twice weekly for 14 weeks, by topical application to the skin of the back) showed strong perifollicular melanocyte activation within 24 hour, and the entire middle and upper layers of the dermis were populated with dihydroxyphenylalanine oxidase-positive (dopa oxidase-positive) melanocytes within 6 days, spreading to involve all the interfollicular zones and the entire basal epidermis by the end of 2 weeks. Dermal nevi were evidenced by the end of 6 weeks and dopa oxidase-positive, melanocytic, intradermal tumors were present by the end of 2-3 mo., as were other, unrelated tumors including papillomas, keratoacanthomas and carcinomas. Application of croton oil DAB 6 in the same conc. and dosage (for the same length of time) stimulated formation of dopa oxidase-positive melanocytes in the deep corium, not extending to either the basal or the upper epithelial cells and without either nevus or tumor formation. Application of 1,2-benzanthracene in the same conc. and dosage but for 6 weeks, only, resulted in the appearance of some melanocytes in the perifollicular areas of the deep and middle layers of the dermis.

70-1068 FAILURE TO PRODUCE TUMOURS IN CATTLE
WITH 20-METHYLCHOLANTHRENE AND 3,4-
BENZPYRENE. (E.) Datta, S. P. (U. Wisconsin-

Parkside, Kenosha) and T. Ghose, *Experientia* 26(1):78-79, 1970.

Five young calves (Jersey and Friesian breed) received 3-methylcholanthrene (MC; 400 mg suspended in olive oil, s.c., followed 315 days later by implantation of a gelatin capsule containing 250 mg powdered MC) or 3,4-benzpyrene (BP; a 5 mg pellet, under the kidney, followed 10 weeks later by another gelatin capsule containing 250 mg MC). The animals were observed for 6-36 mo. No significant changes were observed in any of the animals. Implantation of these BP pellets (5 mg; s.c.) or inj. of an olive oil suspension of MC (10 mg) from the same bottle induced sarcomas in almost 100% of Wistar rats within 9 mo. of exposure.

70-1069 AN EARLY EFFECT OF 7,12-DIMETHYLBENZ
(a)ANTHRACENE ON RAT MAMMARY GLAND
DNA SYNTHESIS. (E.) Tominaga, T. (Roswell
Park Mem. Inst., Buffalo, N. Y.), P. R. Libby
and T. L. Dao. *Cancer Res.* 30(1):118-122, 1970.

Sprague-Dawley rats (55-65-days-old) were admin. 7,12-dimethylbenzanthracene (DMBA; 20 mg, p.o.) phenanthrene (100 mg) and sacrificed at various times. In the females, the incorporation of ³H-thymidine into mammary tissue DNA *in vitro* was inhibited as early as 6 hours after DMBA admin., reaching a peak inhibition at day 4, then returning to the control level at day 6. In males, inhibition was similar to that of females at 24 hours, but the incorporation of labeled thymidine began to rise at day 4, reached control levels at day 6 and was 150% of controls at day 10. DNA polymerase activity in female mammary tissue after DMBA admin. was increased after 1 day, decreased from days 2-7, and rose above control levels at day 8. Autoradiographic technics showed that there were fewer labeled cells in the rats treated with DMBA and the labeled cells incorporated less ³H-thymidine. Treatment with phenanthrene did not produce any significant changes from control values.

70-1070 INFLUENCE OF COHABITATION ON MAMMARY
CARCINOGENESIS BY 7,12-DIMETHYLBENZ-
ANTHRACENE IN THE FEMALE RAT. (Fr.) Guillon,
J.-C. (Pasteur Inst., Paris), A. Gentil, C.
Lasne and I. Chouroulinkov. *C. R. Acad. Sci.
[D] (Paris)* 270(7):1066-1068, 1970.

Female Sprague-Dawley rats were treated with 7,12-dimethylbenzanthracene (15 mg, single forced p.o. dose in olive oil), then divided at random and placed in 30 individual cages or 5 collective cages (containing 10 rats each). All survivors were sacrificed at the end of a 16-week observation period. The only significant difference found between the isolated rats and rats living in the collective cages was in mean tumor wt. among survivors at the end of week 16: 4.0 ± 0.8 and 2.0 ± 1.0 resp. (significance at

a 5% level of confidence). No significant differences were seen in the mortality rate (despite some temporary variations) body wt., adrenal wt., the number of tumors observed at the end of the study, tumor sites or tumor histology.

10-1071 EFFECT OF SURGICAL TRAUMA ON 7,12-DIMETHYL BENZANTHRACENE INDUCED BREAST CANCER IN THE SPRAGUE-DAWLEY RAT. (E.) Davidson, A. (U. North Carolina Sch. Med., Chapel Hill), C. G. Thomas, Jr. and J. Owen. Surg. Forum 20:105-106, 1969.

The incidence of breast tumors in female Sprague-Dawley rats receiving an intragastric dose of 7,12-dimethylbenzanthracene (DMBA; 20 mg) at 50 days of age was 43%; in rats undergoing partial mastectomy at age 40 days, then DMBA admin. at age 50 days, the tumor incidence was 69%; and in rats receiving DMBA at age 50 days and partial mastectomy at age 60 days, the incidence of breast tumors was 73%. The number of tumors/rat in the non-traumatized and traumatized areas were 1.9 and 1.6, resp., in the second group of rats; in the third group they were 1.2 and 2.5.

10-1072 THE EFFECT OF COLD STRESS ON CHEMICAL CARCINOGENESIS OF RAT SALIVARY GLANDS. (E.) Turbner, S. (Tufts U. Sch. Dent. Med., Boston, Mass.), G. Shklar and E. Cataldo. Oral Surg. 29(1):130-137, 1970.

11lets of 7,12-dimethylbenzanthracene were implanted in the right submandibular gland of 48 albino rats (200-250 g) and 24 were placed in a room maintained at 3°C for 19 weeks. All rats developed tumors, palpable at 11 weeks, in the right submandibular gland, but by week 13, tumors in the cold-stressed rats were larger and the rats weighed an av. of 81 g less at time of death. Microscopically, the tumors were epidermoid carcinomas and histologically similar in both groups.

10-1073 VARIATIONS IN EXPERIMENTAL CARCINOGENESIS OF SUBMANDIBULAR GLAND IN THREE STRAINS OF RATS. (E.) Turbner, S. (Tufts U. Sch. Dent. Med., Boston, Mass.) and G. Shklar. Arch. Oral Biol. 14(9):1065-1071, 1969.

11lets of 7,12-dimethylbenzanthracene were implanted in the right submandibular glands of Sprague-Dawley, Wistar, and Long-Evans rats (5 animals each), and starting at 6 weeks, 2 animals of each strain were sacrificed weekly. The sequence of events leading up to carcinoma was the same in each strain: degeneration and necrosis around the pellet, becoming a band of line-like material; proliferation of duct-like structures within the band, becoming cysts; and cystic epithelium giving rise to epidermoid carcinomas in all cases. By 7 weeks, the Long-

Evans rats demonstrated dysplasia and early cancer, while the other 2 strains had only cystic changes. The Sprague-Dawley rats had a more advanced epithelial proliferation than the Wistar strain for up to 8 weeks. At 9 weeks, a well-defined carcinoma was seen in the Long-Evans rats, while carcinomas seemed to be developing in the other strains. After week 11, all 3 had histologically-similar, well-developed carcinomas of the submandibular gland. No relationship of tumor size to strain was observed.

10-1074 EFFECT OF 9,10-DIMETHYL-1,2-BENZANTHRACENE ON THE MOUSE OVARY. OVARIAN TUMORIGENESIS. (E.) Krarup, T. (Finsen Inst. Lab., Copenhagen). Brit. J. Cancer 24(1):168-186, 1970.

Mature and immature female virgin Bagg-strain mice were admin. 7,12-dimethylbenzanthracene (0.25-1.0 mg, i.p. or p.o.). The early changes were a reduction in the numbers of oocytes and follicles, with an increase in stromal mass, especially in the i.p.-treated animals. These changes progressed to a preneoplastic state, characterized by a diffuse luteinization of the ovarian parenchyma. Neoplastic development was correlated with elimination of germ cells, as tumors occurred faster in i.p.-treated animals. Also, mice treated orally at 4 mo. had a shorter tumor latency and a faster reduction of oocytes than animals treated orally at 21 days. Luteomas, micro- and macroscopic granulosa cell tumors of the ovary were observed; and when the microscopic granulosa tumors grew to macroscopic size, the contralateral ovary atrophied. Total tumor incidence at 6 mo. of mice treated at 21 days, was 13/27 treated p.o. and 19/28 treated i.p. Proliferation patterns of the tumors were determined by ³H-thymidine inj.

10-1075 RELIABILITY OF EXFOLIATIVE CYTOLOGY IN INDUCED CARCINOMA IN HAMSTER'S POUCH. (E.) Hanks, C. T. (State U. New York Health Sci. Ctr., Buffalo), A. P. Chaudhry and M. E. Neiders. Acta Cytol. (Balt.) 13(2):94-98, 1969.

The right cheek pouches of 3-4-mo-old golden Syrian male hamsters were painted with 7,12-dimethylbenzanthracene (about 0.05 ml of 0.5%; 2 admin./week), each hamster receiving 12-48 applications. The lesions were identified as frank carcinoma, carcinoma in situ, or leukoplakia in 50 hamsters; the remaining 40 were normal, hyperkeratotic or hyperplastic. Cytologic smears (4/hamster) were read by 3 investigators as 12%, 11% and 16% false negatives from the smears diagnosed as suspicious or malignant; and 13%, 30% and 12.5% false positives from the non-malignant group of smears. When the diagnosis was based on the 4 smears from the individual animal, there were 0-4% false negatives, and 30-42.5% false positives. Overall agreement between the 3 investigators was 88%.

70-1076 THE EFFECT OF CASTRATION ON CHEMICAL CARCINOGENESIS IN THE CHEEK POUCH OF THE MALE SYRIAN GOLDEN HAMSTER. (E.) Levij, I. S. (Hebrew U. Hadassah Med. Sch., Jerusalem), A. Durst and A. Pollack. Oral Surg. 28(5): 709-712, 1969.

The right cheek pouch of intact or orchiectomized (orx.) male golden Syrian hamsters (1-1.5-mo-old, 55-65 g) was painted with 0.5% 7,12-dimethylbenzanthracene (3 doses/week) for up to 16 weeks. There was no difference between the pouches of the intact and orx. animals up to week 12. After 4 weeks, a mild irregularity of the mucosa, with moderate acanthosis and marked hyperkeratosis, was seen in the treated pouches. At 8 weeks, each rat in the group had a benign papilloma with areas of atypical epithelium. After 12 weeks, 1-4 tumors/pouch were observed, with foci of intraepithelial and infiltrating squamous cell carcinoma. At 16 weeks, cheek pouches of the orx. hamsters had 2-4 squamous cell carcinomas (5-12 mm), while the intact animals had 4-12 tumors (8-15 mm) in each pouch.

70-1077 DMBA SKIN CARCINOGENESIS IN ADULT MICE THYMECTOMIZED AT BIRTH. (E.) Borum, K. (Univ. Hosp., Lund, Sweden). Ann. Ital. Derm. Sif. 22(4):371-374, 1968.

Newborn NMRI mice were thymectomized or sham-operated; 7 weeks later, 7,12-dimethylbenzanthracene (0.05 ml of a 0.25, 0.5, or 1.0% soln.) was painted on the dorsal skin. The combined incidence of papillomas at all 3 dosage levels was 14/23 (61%) for the thymectomized females and 5/24 (21%) for thymectomized males. No difference was noted, however, between the incidence or the latent period (all within 35-53 days) between thymectomized and sham-operated animals of the same sex; 3/19 (16%) of the male sham-operated mice and 13/21 (62%) of the females developed papillomas.

70-1078 TESTS ON THE EXPERIMENTAL INDUCTION OF CANCER. (E.) Kantemir, I. (Ankara U. Med. Sch. Inst. Oncol., Turkey). Acta Med. Turc. 6(1):3-10, 1969.

Albino mice were painted with 7,12-dimethylbenzanthracene (DMBA) 3,4-benzpyrene (BP), or 3-methylcholanthrene (MC) (0.2% soln.; 1 admin. every 3 days of 1.25 mg active substance). After 40 treatments, all mice painted with DMBA had developed tumors, as compared to only 2 mice treated with BP; MC and acetone alone did not induce any tumors up to 130 days. DMBA accelerated tumor initiation by MC and BP.

70-1079 DIMETHYL SULPHOXIDE (DMSO) ABOLISHES THE CARCINOGEN-PROVOKED CYTOPLASMIC BARRIER OF MALIGNANT EPIDERMAL CELLS. AN ELECTRON MICROSCOPIC STUDY WITH SKIN-TUMOR-

RESISTANT MICE. (E.) Stjernvall, L. (U. Helsinki). Ann. Med. Intern. Fenn. 47(4): 253-258, 1969.

Normal skin, skin with Tween-60-induced benign epidermal hyperplasia, and skin with 7,12-dimethylbenzanthracene-induced malignant epidermal hyperplasia from 3-mo.-old female skin-tumor-resistant RA mice, was examined by the electron microscope for the response to treatment with vinblastine sulfate (85 μ ; 3 admin. in 3 successive days). The normal and benign hyperplastic skin showed a decrease of ground cytoplasm, branching tubules and/or vesicular formations, a decrease in tonofibrils and filaments, and an increased branching of tubules and cisternae of the endoplasmic reticulum. The malignant hyperplastic epithelium was resistant to the effects of vinblastine dissolved in acetone, but gave a characteristic response (as above) when dimethyl sulfoxide was used as the carrier.

70-1080 MEDIASTINAL LYMPHOMAS IN SWISS MICE RECEIVING URETHAN X. A CYTOPHOTOMETRIC STUDY OF DNA IN LEUKEMIC CELLS IN GRAFTED ANIMALS. (Fr.) Cappelaere, P. (Inst. Cancer Res., Lille, France), M. d'Hooghe and J. Driessens. C. R. Soc. Biol. (Paris) 163(10): 2151-2153, 1969.

Neonatal Swiss mice received i.p. implant of cells of a mediastinal lymphoma induced in the donor by urethan, and were sacrificed 8 days later in the presence of demonstrable hepatosplenomegaly and extensive lymphadenopathy. The mean value for DNA in leukemic cells in the peripheral circulation was 18.17 arbitrary units (AU; representing an increase of approx. 60%, as compared to homologous normal cells). In the spleen, it was 18.78 AU, as compared to 11.15 AU in the normal spleen of mice of the same age. Lymphocytes with diameters of less than 10 μ constituted 7-8% of the cells in the peripheral circulation, with an absolute number of approximately $14 \times 10^3/\text{mm}^3$. Comparable tabulations for normal animals of the same age were 45% and $3.2 \times 10^3/\text{mm}^3$. The mean DNA value for these small lymphocytes was 13.87 AU (DNA value in normal animals not specified).

70-1081 MODIFICATION OF URETHAN-LUNG TUMOR INCIDENCE BY LOW X-RADIATION DOSES, CORTISONE, AND TRANSFUSION OF ISOGENIC LYMPHOCYTES. (E.) Cole, L. J. (Naval Radiol. Defense Lab., San Francisco, Calif.) and W. A. Foley. Radiat. Res. 39(2):391-399, 1969.

Male (C57L x A)F₁ hybrid, 2-3-mo.-old mice were X-irradiated, then 1 day later given urethan (0.08 - 0.2 mg/g i.p.) and/or cortisone acetate (2.5 mg; 7 inj. s.c. on alternate days). Mice receiving irradiation and urethan had the highest incidence of lung tumors (50%) compared

mice irradiated only (12.5%) and mice receiving urethan only (16%). Cortisone plus X-irradiation resulted in an incidence of 42%, and urethan plus cortisone gave 37% (not significant). When the irradiation was fractionated (over 6 days) and urethan given, lung tumor induction was additive. A single dose of radiation and urethan was not additive and fractionated irradiation alone did not increase the incidence. Amino-thylisothiuronium bromide, given 15 minutes prior to irradiation, and urethan resulted in an increased incidence of lung neoplasms. Isogenic lymph node lymphocytes and peripheral blood leukocytes given 2 days after irradiation and urethan reduced the incidence of lung tumors by a factor of 2.

0-1082 PULMONARY ADENOMAS IN SWISS MICE RECEIVING URETHAN. VI. EFFECTS OF BUTYL AND ISOAMYL CARBAMATES. (Fr.) Lespagnol, J. (Inst. Cancer Res., Lille, France), L. Adenis, J. C. Cazin and J. Driessens. C. R. Soc. Biol. (Paris) 163(10):2145-2147, 1969.

Among Swiss mice receiving urethan (100 ppm, p.o. in drinking water for 16 weeks), 18/18 developed pulmonary tumors, with a mean of 19 tumors/animal. Comparable tabulations for butyl carbamate (200 ppm, as above) were 11/24 and 1, resp.; for the same dose of isoamyl carbamate, 27/40 and 2, resp.; for urethan + butyl carbamate (both as above), 22/22 and 11, resp.; for urethan + isoamyl carbamate, 35/35 and 13, resp. The indicated differences of mean tumor number, as between urethan alone and urethan + butyl or isoamyl carbamate, were not statistically significant. It is concluded that the 2 carbamate compounds, like p-aminobenzoic acid in a previous study, showed neither carcinogenic nor anti-urethan activity, in contrast to the strong anti-urethan effect of sulfanilimide in the previous study.

0-1083 PULMONARY ADENOMAS (VII) AND MEDIASTINAL LYMPHOMAS (IX) IN SWISS MICE RECEIVING URETHAN. INFLUENCE OF NEONATAL THYMECTOMY. (Fr.) Adenis, L. (Inst. Cancer Res., Lille, France), M. N. Vlaeminck and J. Driessens. C. R. Soc. Biol. (Paris) 163(10):2147-2150, 1969.

Among Swiss mice thymectomized within 24 hr. after birth, and beginning treatment with urethan at the age of 3 weeks (100 ppm, p.o. in drinking water for 10 weeks), 13/93 survivors developed nodal, diffuse, visceral, malignant lymphomas, including 7/13 with lymphocytic-lymphoblastic lymphatic tumors (with extensive visceral dissemination) and 6/13 with lymphocytic-lymphoblastic lymphatic tumors, also widely disseminated. Survival times were 6-10 mo. and 7-14 mo., resp. Lymphatic tumors appeared to have developed from remains of incomplete thymectomy, reducing the percentage incidence of malignant lymphomas attributable to urethan to approx. 7% (6/87),

compared to 47% among mice treated with urethan alone. Death due exclusively to lung tumors was seen in 66/93. Tumors in this group were greater in number/animal and much more extensive than those found in animals receiving urethan alone, which frequently involved an entire lung or showed massive foci of tumor cells in alveolar cavities at some distance from tumor nodules (although no distant metastasis was found). Death in 11/93 was due to hepatosplenic hemangiomatosis with intraperitoneal hemorrhage; 3/39 died from mammary carcinoma.

70-1084 A NON-RADIOACTIVE PHOTOCHEMICAL MODEL FOR POLYCYCLIC AROMATIC HYDROCARBON-INDUCED CARCINOGENESIS. (E.) Buu-Hoï, N. P. (Nat. Ctr. Sci. Res., Paris) and S. S. Sung. Naturwissenschaften 57(3):135, 1970.

The early reaction between a carcinogen and cell substrate may be a photochemical one and the energization of this type of reaction in the absence of light may be due to a biochemoluminescent reaction. The potentiation of the carcinogenicity of 3,4-benzpyrene after irradiation with light, and also the excitation energies generated by the thermodecomposition of 2-oxaoxetanes and the luminescence produced by the oxidation of polycyclic hydrocarbons or the decomposition of their peroxides are discussed.

70-1085 A GAS CHROMATOGRAPHIC DETERMINATION OF BENZO(a)PYRENE USING ELECTRON CAPTURE. (E.) Duncan, R. M. (Aluminum Co. of Canada, Ltd., Arvida, Quebec). Amer. Industr. Hyg. Ass. J. 30(6):624-629, 1969.

A method for detecting air pollution by 3,4-benzpyrene (BP) is described. BP was separated from other hydrocarbons and analyzed in a Varian Aerograph gas chromatograph using a 10-foot by one-eighth inch stainless steel column packed with 40% sodium chloride (48-65 mesh) and 60% Chromosorb G (60-80 mesh) coated with 2% SE-30. UV fluorescence analysis showed accuracy within 5%. Analysis can be done in 15 min.; other components can be analyzed simultaneously; and the electron capture detector enables collection of the separated components. This method could detect as little as 10^{-9} g/200 μ l of the BP.

70-1086 EFFECT OF DISCHARGES FROM OIL PROCESSING PLANTS ON POLLUTION OF SOIL AND VEGETATION BY 3,4-BENZPYRENE. (E.) Shcherbak, N. P. (Inst. Exp. Clin. Oncol., Moscow). Hyg. Sanit. 33(7-9):109-112, 1968.

Soil and vegetation samples were taken from 4m² areas at distances 100-3000 meters from an arbitrary center near the "Neftegaz" factory, which discharges large quantities of 3,4-benzpyrene (BP) into the air. Zones closest to the center had the highest conc. of BP (19.5-

22.1 mg/kg), which decreased with distance and according to prevalent wind conditions. The level in the eastern direction at 3000 meters was 1.57 mg BP/kg, compared to a background city level of 0.4. The pollution to the north reached background levels at about 2000 meters and at 750 meters to the south; other sources of pollution were to the west. Washing the vegetation in hot running water for 30 min. reduced the BP content 50-66%.

70-1087 ENVIRONMENTAL CARCINOGENS. THE MODIFYING EFFECT OF COCARCINOGENS ON THE THRESHOLD RESPONSE. (E.) Bingham, E. (U. Cincinnati Coll. Med., Ohio) and H. L. Falk. Arch. Environ. Health (Chicago) 19(6):779-783, 1969.

Various conc. of 3,4-benzpyrene (BP), dissolved in decalin or n-dodecane-decalin, or benzanthrane (BA), in toluene or n-dodecane, were applied to the skin of C3H/He mice (50 mg by vol., 3 admin./week). Conc. of BP below 0.02% in decalin induced no tumors, while 0.00002% in n-dodecane-decalin produced an incidence of 21%. Similar results were obtained with BA. When BP was dissolved in 1-dodecanol (0.05-0.2% in 0-100% of the cocarcinogen), the latent period of tumor induction decreased from 40 to 20 weeks as the conc. of the cocarcinogen increased, but max. effectiveness was at the lowest conc. of BP. The conc. of BP had no effect when 1-phenyldodecane was used as the cocarcinogen.

70-1088 INTERACTION OF NUCLEIC ACIDS. V. CHEMICAL LINKAGE OF 3,4-BENZPYRENE TO DEOXYRIBONUCLEIC ACID IN AQUEOUS SOLUTION. (E.) Lesko, S. A., Jr. (Johns Hopkins U., Baltimore, Md.), P. O. P. Ts'o and R. S. Umans. Biochemistry (Wash.) 8(6):2291-2298, 1969.

Chemical reactions between 3,4-benzpyrene (BP) and DNA were carried out in neutral, aqueous soln. at room temperature; data were consistent with the formation of a covalent linkage between BP and DNA. This linkage was induced by reacting the physical complex with I_2 , H_2O_2 in the presence and absence of ferrous ion, and the ascorbic acid model hydroxylating system. Up to 40% of the physically-bound BP was linked covalently to the DNA under appropriate conditions. Under the same conditions, 1,2-benzpyrene was linked to DNA only to a very limited extent. The covalently-linked BP could not be extracted by organic solvents that removed over 99% of the physically-bound BP from DNA. The chemical linkage was further characterized by sucrose gradient electrophoresis and gel filtration of the chemical complex before and after enzymatic hydrolysis. The results indicate that BP free radicals (possibly cationic) may be involved as intermediates in the reactions.

70-1089 ROLE OF VITAMIN A IN CARCINOGENESIS. (E.) Saffiotti, U. (NCI, Bethesda, Md.). Amer. J. Clin. Nutr. 22(8):1088, 1969.

In golden Syrian hamsters, 3,4-benzpyrene induction of squamous metaplasia and squamous cell carcinoma in the tracheobronchial mucosa and squamous cell papillomas of the forestomach were inhibited when followed by p.o. admin. of vitamin A palmitate. It is possible that there is a common mechanism for carcinogens and vitamin A which act in opposite directions.

70-1090 BENZPYRENE PRETREATMENT CHANGES THE KINETICS AND pH OPTIMUM FOR ANILINE HYDROXYLATION IN VITRO, BUT NOT THOSE FOR BENZPHETAMINE DEMETHYLATION IN VITRO BY RAT LIVER MICROSOMES. (E.) Rickert, D. E. (U. Iowa Coll. Med., Iowa City) and J. R. Fouts. Biochem. Pharmacol. 19(2):381-390, 1970.

The pH optimum for *in vitro* metabolism of aniline, but not benzphetamine or 3,4-benzpyrene (BP) by rat liver microsomes, was shifted (from 7.0 to 8.1) after pretreatment of Sprague-Dawley rats with BP (45 mg/kg). The spectral dissociation constants (K_s) of aniline, comparing values at pH 7.0 and 8.1, were similar for hepatic microsomes from control rats but different, for microsomes from BP-treated rats. The absorbance from peak to trough of the spectrum differed in preparations from control and treated rats. The Michaelis constant (K_m) for BP hydroxylation was increased 2.5-fold, and the max. velocity (V_{max}) tripled in BP-treated rats; the K_s , K_m and V_{max} for benzphetamine were unchanged by BP treatment. For aniline hydroxylase, the K_m was doubled when the pH changed from 7.0 to 8.1 in both control and treated preparations, and the V_{max} was increased by BP treatment when measured at pH 8.1.

70-1091 STUDIES ON THE HYDROXYLATION OF 3,4-BENZPYRENE BY HEPATIC MICROSOMES. EFFECT OF ALBUMIN ON THE RATE OF HYDROXYLATION OF 3,4-BENZPYRENE. (E.) Alvares, A. P. (Burroughs Wellcome Co. Res. Labs., Tuckahoe, N. Y.), G. Schilling, A. Garbut and R. Kuntzman. Biochem. Pharmacol. 19(4):1449-1455, 1970.

The supernatant or microsomes of liver from male Sprague-Dawley rats (130-150 g) inj. with 3-methylcholanthrene (MC); 20 mg/kg) were analyzed for 3,4-benzpyrene (BP) hydroxylase activity. The formation of enzyme was linear with respect to tissue conc. when supernatant from less than 10 mg liver was used as enzyme source, but not when microsomes from 2-40 mg liver were used. The latter system became linear with addition of 0.4 or 0.6 mg albumin. The Michaelis constant (K_m) for hydroxylation of BP was significantly different for the MC-treated rats and the max. velocity (V_{max}) was tripled. Addition of albumin or microsomes to the enzyme reaction mixture resulted in increased solubilization of BP.

70-1092 THE EFFECT OF PROLONGED PRETREATMENT WITH 6-SUBSTITUTED BENZO[a]PYRENE

DERIVATIVES UPON ZOXAZOLAMINE PARALYSIS TIMES IN MICE. (E.) Dewhurst, F. (Leicester Polytechnic, England) and D. A. Klitchen. Biochem. Pharmacol. 9(2):615-617, 1970.

Groups of 10 mice were inj. with either arachis oil or 6-substituted benzpyrene (BP) derivatives in arachis oil, and again in 72 and 96 hours. The zoxazolamine paralysis time was measured 24 hours later. It was found that 6-hydroxymethyl-BP, 6-methyl-BP and BP-6-carboxaldehyde produced a highly significant prolongation of paralysis time. This effect is thought to be due to the production of a metabolite capable of inducing *in vivo* inhibition of liver microsomal "drug-metabolizing" enzyme activity.

10-1093 DIFFERENCES IN THE AMOUNTS OF HYDROCARBONS APPEARING IN PURE CULTURES OF Bacillus badius AS A CONSEQUENCE OF THE PRESENCE OF VARIOUS CHEMICAL COMPOUNDS IN THE CULTURE MEDIUM. (Fr.) Niaussat, P., C. Auger and L. Allet. C. R. Acad. Sci. [D] (Paris) 270(7): 042-1045, 1970.

Peptone broth (free of 3,4-benzpyrene (BP) or erylene (P) at the start of the experiment) inoc. with an 18-hour culture of Bacillus badius was incubated at 37°C for 7 days in the dark, with lycopene, β -carotene, sodium acetate, or hydrosoluble vitamin K₁ (10 mg/liter) or with naphthalene-acetic acid (0.1 mg/liter). With the 7-day BP content (0.084 μ g/l) of a control broth containing B. badius alone taken as 100%, the BP contents of the test broths were 146%, 17%, 70%, 142% and 161%, resp. Comparable calculations for P (control = 0.30 μ g/l) were 57%, 103%, 83%, 123% and 138%, resp. The proportional relationship of P to BP, in turn, is 3.6 (control), 3.9, 3.2, 4.24, 3.07 and 3.08, resp. It was concluded that the content of the substrate had a significant effect on the quantity of hydrocarbons produced by B. badius cultured *in vitro*. It was also suggested that naphthalene-acetic acid and vitamin K₁ may act as precursors of BP biosynthesis *in vivo*.

10-1094 THE EFFECTS OF CASTRATION ON THE INDUCTION OF EXPERIMENTAL GLIOMAS IN MICE. (E.) Hopewell, J. W. (Churchill Hospital, London). Brit. J. Cancer 24(1):187-190, 1970.

Slits of 3,4-benzpyrene were deeply implanted to the brains of 4-6-week-old Sprague-Dawley rats, such that they involved the sub-ependymal area of the lateral ventricle. Half the rats were orchietomized (orx.) at this time. Glial tumors of various types developed later in only 3 (50%) of the orx. animals, as compared to 9 (77.8%) of the intact rats.

10-1095 PESTICIDE SYNERGISTS AND THEIR METABOLITES: POTENTIAL HAZARDS. (E.)

Falk, H. L. (NCI, Bethesda, Md.) and P. Kotin. Ann. NY Acad. Sci. 160(1):299-313, 1969.

Pesticide synergists are discussed concerning their inhibition of enzyme systems which metabolize known carcinogens. Various conc. and routes of admin. of compounds with the methylenedioxybenzene structure in the molecule (piperonyl sulfoxide and butoxide) inhibited the biliary excretion of 7,10-¹⁴C-benzpyrene (BP; 400 μ g inj. i.v.) in Sprague-Dawley rats. The Sprague-Dawley strain, especially the females, was affected more than NIH black rats. These compounds also enhanced Freon-induced hepatoma in newborn mice. Simpler derivatives (safrole, 0.6 mM/kg i.v.; Tropital, 0.4 mM/kg i.v. and 2.7 mM/kg p.o.) also inhibited biliary excretion of labeled BP.

70-1096 TUMORIGENICITY OF VERY FRESH TOBACCO SMOKE CONDENSATE TO MOUSE SKIN. (E.) Davies, R. F. (Tobacco Res. Council Labs., Harrogate, England). Brit. J. Cancer 23(4): 858-860, 1969.

Of 4-6-week-old female albino mice treated with cigarette smoke condensate (3 admin./week x 56 weeks), 37.3/100 developed tumors after application of 50 mg of condensate (from a Capillary Press within 2-3 seconds of each puff) to the interscapular area, 42.7/100 for a 4-hour condensate to the interscapular area and 18/100 for a 4-hour condensate to the whole back. There was no significant difference in mouse skin tumorigenicity between condensates applied within 2 seconds or 4 hours of smoking when equal amounts were applied to a similar area of skin. The application of either condensate to the interscapular area was more tumorigenic than the same amount of 4-hour-old condensate applied to the whole length of the back (interscapular, 6.7 mg/cm²; whole back, 2/3 mg/cm²).

70-1097 A STUDY OF THE EFFECTS OF ALTERING THE TAR/NICOTINE RATIO IN EXPERIMENTAL TOBACCO CARCINOGENESIS. (E.) Davies, R. F. (Tobacco Res. Council Labs., Harrogate, England) and J. K. Whitehead. Brit. J. Cancer 24(1): 191-194, 1970.

The skin of female, 4-6-week-old albino mice was treated topically with non-volatile whole-smoke condensate (25, 50 or 100 mg; 3 admin./week for life) from plain cigarettes or cigarettes specially prepared to produce a high nicotine content while filtering out tars. The tar/nicotine ratio in the whole smoke condensates was 14.7:1 for the plain cigarettes and 11.2:1 for the special filtered cigarettes. Examination of animals at 64 and 128 weeks showed no significant difference between the incidence of tumor- and carcinoma-bearing mice in the groups treated with a low tar/nicotine ratio and the others.

70-1098 COMPARATIVE CARCINOGENICITY FOR MOUSE-SKIN OF SMOKE CONDENSATES PREPARED FROM CIGARETTES MADE FROM THE SAME TOBACCO CURED BY TWO PROCESSES. (E.) Roe, F. J. C. (Chester Beatty Res. Inst. Cancer Res., London), J. C. Clack, D. Bishop and R. Peto. Brit. J. Cancer 24(1):107-121, 1970.

Smoke condensates were prepared from standardized cigarettes containing flue-cured and redried (FC) or air-cured and bulk-fermented (AC) tobacco and applied to the dorsal skin of female Swiss mice (60 mg of each in acetone; 3 admin./week). The incidence of skin tumors for the FC-treated group was 208/400, for the AC-treated group 270/400, and 5/400 for controls treated only with acetone; but there was a significant difference in the development of malignant tumors in the FC group (119) and the AC group (93). There was also a significant difference in the incidence of inflammatory ulcers and the rate of detection of lung tumors, but this difference may be because more FC cigarettes were used to produce the same amount of condensate. There was no effect on the incidence of other neoplasms including lymphomas.

70-1099 STUDIES ON THE EFFECT OF RESERPINE THERAPY ON THE FUNCTIONAL CAPACITY OF THE TRYPTOPHAN-NIACIN PATHWAY IN SMOKER AND NON-SMOKER MALES. (E.) El-Zoghby, S. M. (Med. Res. Inst., Alexandria, Egypt), A. K. El-Shafei, G. A. Abdel-Tawab and F. S. Kelada. Biochem. Pharmacol. 19(5):1661-1667, 1970.

The 24-hour urine samples, from a group of 16 males who had smoked more than 6 cigarettes/day for more than 2 yr., after oral loading with 2 g L-tryptophan, contained significant amounts of anthranilic acid glucuronide, o-aminohippuric acid, kynurenic acid, acetylkynurenine, kynurenine, 3-hydroxykynurenine and xanthurenic acid, as compared to the urine of 14 non-smoker males. Admin. of pyridoxine hydrochloride (120 mg p.o.) reduced the level of some metabolites to that of the controls. A qualitatively and quantitatively similar excretion pattern was seen in smokers (13) and non-smokers (7) after admin. of reserpine (Serpasil; 0.5 mg daily for 3 days, p.o.).

70-1100 THE AETIOLOGY OF BLADDER TUMOURS. (E.) Schlegel, J. U. (Tulane U. Sch. Med., New Orleans, La.), G. E. Pipkin and G. N. Shultz. Brit. J. Urol. 41(6):718-723, 1969.

The chemiluminescence of urine from 43 non-smokers, 36 smokers, and 6 bladder tumor pts. was investigated by treating a 0.1 ml sample, collected in a dark bottle, with hydrogen peroxide (0.02 ml of 30% soln.) in a Dupont Luminescent Biometer. A significant difference was observed between the chemiluminescence of the urine from the non-smokers (0.59×10^4 femtolumins) and the urine from both the smokers

(1.24×10^4 femtolumins) and the tumor pts. (1.53×10^4 femtolumins). Most of the bladder tumor pts. were smokers; pts. with hematuria were excluded, since hemoglobin caused increased luminescence. Chemiluminescence was suppressed by admin. of ascorbic acid.

70-1101 EXPERIMENTAL PULMONARY CARCINOGENESIS WITH ASBESTOS. (E.) Stanton, M. F. (NCI, Bethesda, Md.), R. Blackwell and E. Miller. Amer. Indust. Hyg. Ass. J. 30(3):236-244, 1969.

No signs of lung tumors were observed in female Osborne-Mendel rats (8-12 weeks old), either in response to pulmonary infarcts induced by hexachlorotetrafluorobutane (0.05 ml i.v., containing 1 mg pulverized asbestos) or when asbestos (5 mg) in equal parts of beeswax and tricaprillin (0.05 ml) was inj. directly into the lung. A third experiment, applying fibrous glass pads (30 x 20 x 3 mm) saturated with a gelatin suspension of asbestos to the surface of the left lung and pericardium, induced mesothelial sarcomas in 22/30 rats (over 50% were located on the pericardial mesothelium); no neoplasms developed using glass pads alone.

70-1102 PREVALENCE OF "ASBESTOS" BODIES IN HUMAN LUNGS AT NECROPSY. (E.) Dicke, T. E. and B. Naylor (1335 Catherine St., Ann Arbor, Mich.). Dis. Chest 56(2):122-125, 1969.

Lung scrapings (700) were made from the base of each lobe of the lungs and from the hilar lymph nodes of 100 autopsied pts. (ages 16-88 yr.). All subjects were residents of Michigan at the time of death. Asbestos bodies were found in 19 (15 men, mostly in the sixth decade); 3 were in both lymph nodes and lungs, and 1 was in the hilar lymph nodes only. Sections of the lung revealed asbestos bodies in 4/19, and in 0/81 in which there was no asbestos bodies in the scrapings. No asbestos bodies were seen in any of the sections of hilar lymph nodes. The pts. showing asbestos bodies had worked at a wide variety of occupations; about 50% of the pts. had lived in the Detroit area, and nearly all of the others in the southern half of Michigan's lower Peninsula.

70-1103 MIGRATION OF ASBESTOS FIBRES FROM SURCUTANEOUS INJECTION SITES IN MICE. (E.) Kanazawa, K. (Chester Beatty Res. Inst. Cancer Res., London), M. S. C. Birbeck, R. L. Carter and F. J. C. Roe. Brit. J. Cancer 24(1):96-106, 1970.

Female, 6-8-week-old, CBA/Lac mice were inj. s.c. with either crocidolite asbestos fibers (10 mg; 0.2-2.0 μ long) once in the right flank or in both flanks (30 mg x 3 days). At autopsy, asbestos fibers were identified by staining tissues with hematoxylin and eosin and micro-incineration technics. Fibers were most

requently found in the ipsilateral axillary lymph nodes, less in the inguinal and mediastinal nodes and not at all in the mesenteric nodes. Axillary nodes from 4 controls inj. only with saline seemed to contain asbestos fibers. Examination of the mesothelial tissues of the first group revealed fibers after 442 days located in the area of thoracic "milky spots." They were also seen in the kidneys by 2 weeks after inj. (but rarely in the liver, brain and lungs), and never in the g.i. tract or pelvic viscera.

1104 AFLATOXIN PRODUCTION IN MEATS. II. AGED DRY SALAMIS AND AGED COUNTRY CURED HAMS. (E.) Bullerman, L. B. (Green Giant Co., Le Sueur, Minn.), P. A. Hartman and J. C. Ayres. *Appl. Microbiol.* 18(5):718-722, 1969.

Salamis were inoc. with conidia (10^2 - 10^6 spores) *Aspergillus flavus* isolated from an Italian-cured salami, and aged under various conditions. Aflatoxins were detected in any salami aged at 10°C ; trace amounts were found in Italian salami aged at 15°C ; and in those aged at 20°C relative humidities above 75%, 1.11 $\mu\text{g/g}$ aflatoxins B₁ + G₁ were formed. No aflatoxins were formed in Hungarian salami (smoked 1 hr./for 8 days after inoc.). In meats smoked or to inoc., aflatoxins were produced only in those aged at 20°C and at a relative humidity 85-90%. *A. flavus* and *A. parasiticus* grew on country-cured hams, but were inhibited by humidities and temperatures, or high salt c.

1105 COUNTRY CURED HAM AS A POSSIBLE SOURCE OF AFLATOXIN. (E.) Strzelecki, H. S. Lillard (Inst. Marine Med., Danzig, Poland) and J. C. Ayres. *Appl. Microbiol.* 18(5):939-939, 1969.

Aspergillus flavus (5 strains), 2 strains of *A. terreus* Wilhelm, 1 strain of *A. tamarii* Kita, and 2 strains of *Penicillium miczynski* Zaleski were isolated from a country-cured ham and tested for aflatoxin production by incubating 10^6 spores in 50 ml yeast extract with 20% sucrose for 7 days at room temperature.

1106 A COMPARATIVE STUDY OF THE EFFECT OF AFLATOXIN B₁ AND ACTINOMYCIN D ON HeLa Cells. (E.) Harley, E. H. (Univ. Coll. Hosp. Sch., London), K. R. Rees and A. Cohen. *Chem. J.* 114(2):289-298, 1969.

The cytotoxic effect of aflatoxin B₁ on a rapidly growing line of HeLa cells was reversible when cells were exposed to up to 40 $\mu\text{g/ml}$ for 2 hours. A dose-related inhibition of the incorporation of ^3H -uridine, ^3H -thymidine, and leucine into RNA (ribosomal and non-ribosomal), and protein, resp., was noted. RNA was

inhibited to the same extent as with actinomycin D (0.2 $\mu\text{g/ml}$), but with a different effect on ribosomal RNA precursors; protein synthesis was more inhibited. Inhibition of protein synthesis as with actinomycin D, was associated with disaggregation of polyribosomes, but it proceeded at a faster rate.

70-1107 THE EFFECT OF AFLATOXIN ON BLOOD CLOTTING IN THE RAT. (E.) Bababunmi, E. A. (U. Ibadan, Nigeria) and O. Bassir. *Brit. J. Pharmacol.* 37(2):497-500, 1969.

Male albino rats (6, wt. about 300 g) consumed a balanced diet (32 g/day x 4) containing mixed aflatoxins (17.5 μg ; B:G = 1.3). Other groups of male rats were inj. i.p. with the aflatoxins extracted from 32 g of the diet, 17.5 μg of pure aflatoxin B₁, or 15 mg 4-hydroxycoumarin. After 3 hr., the aflatoxins had a max. effect on prolonging the blood clotting time whereas the coumarin reached peak activity after 48 hr. The mean clotting time of rats fed the contaminated diet was 47.9 seconds (49.4 and 48.1 seconds in those rats inj. with aflatoxins), compared to 26.2 seconds for control rats; the clotting time in rats inoc. with coumarin was 80.7 seconds.

70-1108 UPTAKE OF AFLATOXIN B₁ BY THE SKIN OF RATS. (E.) Wei, R. D. (Nat. Defense Med. Ctr., Taipei, Taiwan), G. X. Liu and S. S. Lee. *Experientia* 26(1):82-83, 1970.

Sprague-Dawley rats painted with aflatoxin B₁ (AB; 100 $\mu\text{g/d}$ x 50) showed a markedly retarded growth rate compared to controls, with little change in the skin and morphologic changes confined to the liver (focal necrosis, increased large nuclear and binucleolar cells and abnormal nodular lesions, as well as a marked increase in glycogen content in the hepatic cells. In rats painted with a single dose of AB (6.5 μg of AB- ^{14}C), about 50% of the radioactivity was absorbed within 1 hour, and only 20% was present in the skin at 24 hours. The results showed that rat dermis is capable of absorbing AB, and that its toxicity is tissue-specific.

70-1109 THE USE OF TADPOLES OF *Bufo melanostictus* (SCHNEIDER), *Rhacophorus leucomystax maculatus* (GRAY) AND *Uperodon* sp. IN THE BIO-ASSAY OF AFLATOXINS. (E.) Arseculeratne, S. N. (U. Ceylon, Peradeniya), L. M. De Silva, C. H. S. R. Bandunatha, G. E. Tennekoon, S. Wijesundera and K. Balasubramaniam. *Brit. J. Exp. Path.* 50(3):285-294, 1969.

The mean LD₅₀ of aflatoxin B₁ on 15-mm *Bufo melanostictus* larvae was 2.8 $\mu\text{g/ml}$, 1.6 $\mu\text{g/ml}$ on 20-mm *Rhacophorus leucomystax maculatus*, and 0.5 $\mu\text{g/ml}$ on 15-mm *Uperodon*; the LD₅₀ of aflatoxin G₁ was 12.2 $\mu\text{g/ml}$ for *Buf* (15-mm) and 9.3 $\mu\text{g/ml}$ for *Rhacophorus* (20-mm). The smaller larvae,

although more sensitive, were more irregular in their response. Deaths began on day 2 and reached a max. on day 3-4; nuclear and cytoplasmic changes were noted, with necrotic foci in the liver and kidney. Retardation of growth and delay in limb development was observed in those that survived. The LD₅₀ of aflatoxins B₁ and G₁ in chick embryos was 0.58 µg/ml; no cytopathic effect was observed in goat kidney cell cultures treated with up to 7.33 µg aflatoxin.

70-1110 INHIBITION OF AFLATOXIN CARCINOGENESIS BY DIETHYLSTILBESTROL IN MALE RATS. (E.) Newberne, P. M. (Massachusetts Inst. Technol., Cambridge) and G. Williams. Arch. Environ. Health (Chicago) 19(4):489-498, 1969.

Cesarean-derived Charles River rats, about 3 weeks old, were placed on a diet containing aflatoxin B₁ (AB; about 0.2 ppm) and diethylstilbestrol (DSB; 4 mg/kg), and supplied with feed and water ad libitum. Rats receiving DSB + AB weighed 100 g less at 12 weeks, and 200 g less at max. wt. than either the controls or those receiving AB alone. Rats receiving AB and DSB developed a large number of liver nodules (19/40), but had a lower incidence of carcinoma (8/40) as compared to those receiving AB only (25/35); DSB alone resulted in only 1 carcinoma. The decreased tumor incidence was not due to decreased food intake. Adenomas of the pituitary and adrenal were associated with DSB, while adrenal hyperplasia was seen with either or both compounds in the diet. Males were more sensitive to AB than females.

70-1111 HISTOCHEMICAL STUDIES ON THE ACTION OF AFLATOXINS. I. A CYTOLOGICAL AND CYTOCHEMICAL STUDY OF THE LIVER OF RATS FED A DIET CONTAMINATED WITH Aspergillus flavus. (E.) Mietkiewski, K. (Med. Acad., Poznan, Poland), J. Janicki, L. Malendowicz, M. Urbanowicz and B. Filipiak. Folia Histochem. Cytochem. (Krakow) 7(4):379-405, 1969.

Sexually mature male Wistar rats (250-300 g) were fed 20 g/day of wheat contaminated with Aspergillus flavus containing 0.94 mg aflatoxin B₁. After 10 days of feeding, a marked proliferation of bile canaliculi was noted with necrosis of the hepatocytes located peripherally in the lobule, and, especially by day 23, large irregularly-shaped hepatocytes with large nuclei appeared in the region of the central vein. The proliferating oval cells of the bile canaliculi, derived from dedifferentiating hepatocytes, had only slight reactions for acid phosphatase, non-specific esterase, thymine pyrophosphatase and ATPase. The large hepatocytes had large quantities of RNA and glycogen in their cytoplasm and the peripheral degenerating cells demonstrated acid phosphatase and non-specific esterase occurring in cytolysosomes. The enzymes in the hepatocytes near the central vein, however, were normal at day 10.

70-1112 THE INTERACTION OF AFLATOXIN B₁ WITH POLYNUCLEOTIDES AND ITS EFFECT ON RIBONUCLEIC ACID POLYMERASE. (E.) King, A. M. Q. (U. Reading, England) and B. H. Nicholson. Biochem. J. 114(4):679-687, 1969.

The interaction of aflatoxin B₁ (AB) with several polynucleotides was studied spectrophotometrically. Interaction with calf thymus DNA obeyed first-order relationships with an association constant of 0.40 mM⁻¹, but there was evidence for a secondary binding process from results obtained at 390 nm. The spectral shifts decreased in the following order: polyadenylic acid (poly A) + polyuridylic acid (poly U), DNA, poly A, and poly A + polyinosinic acid (poly I). Polycytidylic acid, poly U, poly I (both single- and triple-stranded), AMP, CMP, GMP and UMP did not interact with AB. It is suggested that there is a requirement for the amino group of adenine (or possibly guanine) in order for binding of AB to polynucleotides to occur. Binding was reversed by increasing ionic strength, and by Mn²⁺ and Mg²⁺ in the conc. range 0-5 mM. With both cations and NaCl the reversal was greatest with double-stranded polynucleotides. Inhibition of DNA-dependent RNA polymerase of Escherichia coli by AB in vitro occurred only in the absence of Mg²⁺ and at conc. of Mn²⁺ below the optimum for RNA synthesis in vitro. The degree of inhibition (max. 30%) was dependent on the conc. of Mn²⁺ and decreased during incubation.

70-1113 AFLATOXIN METABOLISM IN MAMMALS. (Fr.) Monjour, L. (Res. Org. African Alimentation Nutr., Dakar, Senegal), R. Giorgi and J. Toury. C. R. Soc. Biol. (Paris) 163(8-9): 2001-2003, 1969.

Protein fractions bound to Aspergillus flavus were not demonstrable by anti-Aspergillus immunoserum in the urine, feces, blood or liver homogenates of rats receiving feed cake contaminated with aflatoxin (0.75 ppm for 14 mo.), rats receiving aflatoxin (5 mg/kg/day x 4, forced p.o. admin.), or of adult monkeys (Papio cynocephalus L.) receiving the same contaminated feed cake for several yr. or fed a diet contaminated by aflatoxin (5 mg/day x 7). Aflatoxin was demonstrable by chromatography in the urine, feces and liver homogenates of the rats treated by forced p.o. admin., only. Neither aflatoxin nor A. flavus protein fractions were demonstrable in the sera of healthy urban and rural subjects (100 each; aged 1-60 yr.), in the sera of 100 pts. chosen at random (40/100 with primary cancers of the liver), or in liver biopsy or autopsy specimens from an unspecified number of traumatized pts., cancer pts. (no details), or pts. dying of viral or bacterial infections. Correlative studies in vitro confirmed that the synergistic action of gastric juice + hydrochloric acid formed a barrier which the protein fractions of A. flavus could not penetrate.

70-1114 OXIDATIVE METABOLISM OF AFLATOXIN B₁ BY MAMMALIAN LIVER SLICES AND MICROSOMES. (E.) Bassir, O. (U. Ibadan, Nigeria) and P. O. Emafo. Biochem. Pharmacol. 19(5): 1681-1687, 1970.

Liver microsomes and liver slices from male goats, sheep, Wistar rats, golden hamsters, mice, guinea pigs, rabbits and dogs were incubated with 160 μ moles aflatoxin B₁ (AB) for 2 hours. The liver slices and microsomes from all animals metabolized the AB into a blue-violet fluorescing substance in UV light, except for the mouse which produced a yellowish-green fluorescing substance (R_F 0.15). The rat and golden hamster also metabolized AB into another yellowish-green fluorescing substance (R_F 0.34); in addition, the hamster tissues also produced a trace amount of the same metabolite as the mouse. The UV absorption peaks and R_F value (0.2) of the blue-violet metabolite were the same as those of aflatoxin M₁. The microsomes of the rat, dog and sheep metabolized AB relatively slowly compared to the others.

70-1115 THE EFFECTS OF AFLATOXIN B₁ AND STEROID HORMONES ON POLYSOME BINDING TO MICROSOMAL MEMBRANES AS MEASURED BY THE ACTIVITY OF AN ENZYME CATALYSING DISULFIDE INTERCHANGE. (E.) Williams, D. J. (Univ. Coll. London) and B. R. Abin. FEBS Letters 4(2):103-107, 1969.

rat liver microsomes, incubated with 40 μ g/ml aflatoxin B₁ (about 4 mg/ml microsomal protein) at 25° C, showed an increase in disulfide interchange activity of about 200%. The RNA:protein ratio decreased, indicating a rise in interchange activity equivalent to the observed increase, and suggesting that ribosomes are displaced from the membrane in complete units. The polysome-depleted membranes, incubated with rat-liver polysomes in the presence of 5mM Mg²⁺, did not regain their ability to bind polysomes. Corticosterone antagonized the action of aflatoxins and increased the polysome binding of the depleted membranes. Corticosterone also enabled binding of polysomes by "smooth" membrane preparations.

70-1116 A KINETIC APPROACH TO A STUDY OF THE INDUCTION OF RAT LIVER MICROSOMAL HYDROXYLASE AFTER PRETREATMENT WITH 3,4-BENZOPYRENE AND AFLATOXIN B₁. (E.) Gurtoo, H. L. and T. C. Campbell (Virginia Polytech. Inst. Coll. Agric., Blacksburg). Biochem. Pharmacol. 19(5):1729-1735, 1970.

microsomal preparation from the livers of Sprague-Dawley rats, 24 hours after i.p. inj. with 3,4-benzpyrene (BP; 10 mg/kg), showed a 14-fold increase in the max. velocity (V_{max}) of BP hydroxylase and a 66% decrease in the Michaelis constant (K_m) for BP; inj. of 20 mg/kg BP caused 23-fold elevation of V_{max} and a 60% decrease K_m ; and inj. of 30 mg BP/kg increased V_{max}

34-fold while K_m was normal. Microsomal protein increased with the increased V_{max} . Inj. of ethionine (700 mg/kg) simultaneously with BP blocked the increase of microsomal protein and BP hydroxylase, but the K_m fell to 10% of the control. When a second dose of BP was admin. 24 hr. after the initial dose, the K_m was reduced while V_{max} remained the same. Aflatoxin B₁ was also shown to stimulate hydroxylase synthesis and activation.

70-1117 CHRONIC OBSTRUCTIVE BRONCHITIS OF THE COAL MINER. EPIDEMIOLOGICAL STUDY OF ITS INCIDENCE IN THE NORMAL POPULATION AND IN COAL MINERS. IMPORTANCE OF EXPOSURE TO DUST AND EFFECT OF SMOKING. (Ger.) Ulmer, W. T. (Inst. Pulmonary Res., Bochum, Germany), G. Reichel and U. Werner. Int. Arch. Gewerbepath. 25(1):75-98, 1968.

An extensive study of 952 steel workers, 626 coal miners without silicosis and 680 miners with silicosis of different grades of severity revealed that dust exposure, although causing increased bronchial irritation, does not necessarily lead to a reduction in lung function. Miners with silicosis of various grades showed no difference in lung function, compared to miners with radiologic signs of lung changes due to dust, and showed no greater incidence in obstructive bronchitis than the non-exposed population. Only miners over 55-yr.-old with advanced silicosis showed a 2-fold increase in the incidence of bronchitis, compared to the general male population. Smoking habits (especially when combined with exposure to dust) had a greater effect on the incidence of obstructive bronchitis than mine dust alone. Heavy smokers (more than 20 cigarettes/day) showed a 30% incidence, non-smokers about 20%. In heavy smokers the bronchial flow resistance and the intrathoracic gas vol. were significantly higher, while arterial oxygen pressure was lower, than in non-smoking controls. Chronic bronchitis was twice as frequent in heavy smokers as in light smokers with the same dust exposure.

70-1118 OCCUPATIONAL ARSENIC INTOXICATION AMONG WORKERS OF THE ARSENIC MINE AND FOUNDRY IN ZLOTY STOK. (Pol.) Juźwiak, J. (Ul. Smoluchowskiego 36, Breslau, Poland). Postepy Hig. Med. Dosw. 23(3):385-412, 1969.

History recorded since 1878 and symptoms of chronic arsenic intoxication in the Zloty Stok area are reviewed and results of a 1960-1961 study of 175 workers (60 miners, 33 foundry workers and 82 other employees) are presented. No neoplasms were detected. The most frequent signs of arsenic intoxication among foundry workers were catarrhal symptoms, coughing, dyspnea, skin changes, intestinal and neurological symptoms; the most frequent among miners were pain in the joints and dyspnea. Foundry workers

frequently had decreased Hb and ESR values, while high Hb and ESR values were found among miners; foundry workers often showed granulocytopenia and a tendency towards lymphocytosis. It is concluded that the main source of chronic arsenic intoxication is water and air pollution in the foundry area.

70-1119 SOME ENVIRONMENTAL CARCINOGENS. (E.)

Case, R. A. M. (Chester Beatty Res. Inst., London). Proc. Roy. Soc. Med. 62(10): 1061-1066, 1969.

A short history was presented of investigations on the carcinogenicity of some aromatic amines (benzidine, α -naphthylamine and β -naphthylamine) used in chemical industries in Britain and on attempts at early diagnosis. Further studies in the rubber industry after antioxidants were removed in 1949 did not show the expected decline in urinary bladder cancer; expected number of deaths involving bladder cancer in this population in 1967-1968 was 4.9, and 16 deaths were found. The use of aromatic amines in other situations such as testing swimming pools for chlorine, testing water for nitrates, and in school chemistry experiments, was considered an unnecessary risk.

70-1120 CHROMOSOME ANOMALIES IN A CASE OF BENZENE LEUKAEMIA. (E.) Hartwich, G. (Med. Clin., Erlangen, Germany), G. Schwanitz and J. Becker. German Med. Monthly 14(9): 449-450, 1969.

A 53-yr.-old man was admitted to the hospital because of increasing physical weakness and frequent fainting attacks. From 1936-1959 he had been a chemical worker in various industries, a wood-worker from 1959-1964, and from 1964-1967 (inclusive), he worked as a compressor operator for an oil refinery, during which time he made simple analyses of the additive "platformate" (normal components, benzene 1-3%, toluene 13-16%, xylene 24-27%, other aromatic components 5-7% by wt.; super components, 8-10%, 20-23%, 20-23%, 7-10% by wt., resp. in open containers. Each analysis took 0.5-1-hour in each shift. There was little or no direct contact. The initial bone marrow examination revealed extensive aplasia with increased myeloblasts; later examinations showed complete infiltration with micro-myeloblasts. Chromosomal anomalies were seen in 20% of the lymphocyte metaphases; all were break phenomena (normal spontaneous rate - 5.5%).

70-1121 THE INTERPLAY OF FACTORS DETERMINING A CANCER PATTERN. (E.) Rose, E. F. (Bantu Cancer Registry, Transkei, South Africa). Progr. Exp. Tumor Res. 12:95-101, 1969.

In the Transkei, South Africa, over 4000 cases of esophageal cancer were reported to the Bantu

Cancer Registry in 14 yr., with a male:female ratio of 5:4. The staple diet of these people is maize, which is deficient in tryptophan and lysine; meat and milk are not part of the regular diet, and eggs are not allowed to most women. The possibility of lowered resistance to natural toxins due to this poor diet is discussed. The toxicity, tumorigenicity, and native uses of Senecio, cycads, berries of Solanum nigrum, tobacco and mycotoxins, as well as other physically irritating foods, is reviewed.

70-1122 OESOPHAGEAL CANCER AND ALCOHOLIC SPIRITS IN CENTRAL AFRICA. (E.)

McGlashan, N. D. (U. Zambia, Lusaka). Gut 10(8):643-650, 1969.

A geographical survey of the distribution of certain selected diseases was made in central Africa, based on recall by hospital superintendents. A seemingly high number of cases of esophageal cancer was noted in eastern Zambia and Malawi. Records from 3 major hospitals indicated that 28.6% of esophageal cancer referrals in Zambia were from the eastern province, although its population was only 14% of the total. A geographical distribution of several environmental factors, showed that inhabitants of this area consumed a certain kind of beer (Kachasu) brewed from sugar and maize husks, as opposed to a cereal-based sugarless grain used by inhabitants of the rest of the country. A variety of equipment, ranging from gun barrels to exhaust pipes, was used for distillation; analysis of spirit samples showed a great range of zinc (0-30.9 mg/liter) and copper (0-40 mg/liter), but no iron, lead or tin. Nitrosamine-like compounds were also found in many samples.

70-1123 RENAL PELVIC CARCINOMA IN A SWEDISH DISTRICT WITH ABUSE OF A PHENACETIN-CONTAINING DRUG. (E.) Angervall, L. (Sahlgren Hosp., Goteborg, Sweden), U. Bengtsson, C. G. Zetterlund and M. Zsigmond. Brit. J. Urol. 41(4):401-405, 1969.

Between 1960 and 1968, transitional cell carcinomas of the renal pelvis were seen in 13 men and 2 women (ages 44-78); 10/13 were inhabitants of Huskvarna and 9 had been employees of a small-arms factory there. Phenacetin abuse (intake of 1 g/day phenacetin for at least 1 yr.) attributed to an analgesic, Hjorton's powder (phenacetin 0.5 g, phenazone 0.5 g, and caffeine 0.15 g), was admitted by 10/13 of the men and periodic use was admitted by 1 man; both women denied phenacetin abuse. Urinary bladder carcinoma also developed in 2 of the pts. with histories of phenacetin abuse.

70-1124 GROWTH AND FREE PROLINE CONTENT OF TOBACCO CALLUS AND HeLa CELLS EXPOSED IN VITRO TO RUBBER DUST AND CARBON BLACK. (E.)

Smith, C. W. (Harding College, Searcy, Ark.), S. H. Wender and C. A. Nau. Amer. Industr. Hyg. Ass. J. 30(4):402-406, 1969.

Tire-rubber dust or carbon black was incorporated into the culture media of tobacco callus (for 5 weeks) or of HeLa cells (for 48-120 hours). Levels of rubber dust greater than 0.5% markedly inhibited tobacco callus growth, and the proline content increased about 30-fold with levels above 10%. Thermal carbon black at high conc. caused a slight inhibition of growth and increased the free proline level, while low conc. of furnace carbon black stimulated growth and high conc. was very inhibitory. Proline levels increased with dosage in the latter case. Rubber dust (200-800 mg/100 ml) was toxic to up to 97% of the HeLa cells and also caused an increase in free proline.

70-1125 BREAST CANCER MANIFEST DURING CONTRACEPTIVE STEROID THERAPY OF TWO WOMEN WITH PRIOR LACTATION MASTITIS. (E.) Meyer, K. K. (Guthrie Clin. Ltd., Sayre, Pa.). Guthrie Clin. Bull (Sayre) 39(1):22-25, 1969.

Contraceptive therapy with norethindrone acetate (1 mg) and ethynylestradiol (0.05 mg) was started on a 42-yr.-old woman after nursing her seventh child. After 18 mo., two 1-cm nodules were palpated in her left breast and interpreted by mammography as benign breast disease. Removal of the breast at 22 mo. revealed a mucinous carcinoma. A second woman (43-yr.-old) was begun on ethynylestradiol (0.1 mg) and dimethisterone (25 mg) with ethinyl estradiol (0.1 mg) sequential therapy. She noted secretions and nodularity in her left breast after 1 yr., but deferred seeking medical treatment until 18 mo. later. The lesion identified as a comedocarcinoma; and a lesion in the breast was identified as an intraductal carcinoma *in situ*. The first woman had had lactation mastitis in the affected breast when she was 24 yr. old, and the second woman had a similar condition of her left breast at age 29.

0-1126 FIBROCYSTIC DISEASE IN WOMEN RECEIVING ORAL CONTRACEPTIVE HORMONES. (E.) Echner, R. E. (Methodist Hosp., Houston, Tex.). Cancer 25(6):1332-1339, 1970.

A review of 258 cases with fibrocystic disease of the breast showed 25/161 premenopausal pts. had been using oral contraceptives for 4 mo.-6 yr. (median 1 yr.) prior to examination. The ages of the 25 pts. ranged from 24-52 yr. (mean 3 yr.), and did not differ significantly from the age distribution of 400 pts. with fibrocystic disease of the breast from 1954-1956, before use of oral contraceptives. The preparation used by 13 of the pts. was primarily estrogenic, 6 used a progestational agent, 9 a combination and 2 a sequential preparation. There was no significant difference in tumor morphology between lesions

in the group on hormonal treatment and the others.

70-1127 ADENOCARCINOMA-LIKE LESION OF CERVIX - A "PILL-INDUCED" PROBLEM? (E.) Talbert, J. R. (Waynesboro Community Hosp., Va.) and J. B. Sherry. Amer. J. Obstet. Gynec. 105(1):117-120, 1969.

A 34-yr.-old, white, married woman (gravida 3, para 3) experienced a single episode of intermenstrual bleeding. She had been taking Enovid (5.0 mg norethynodrel and 0.075 mg mestranol) daily for the previous 4 yr. without significant side effects. Examination revealed an extensive polyploid change of the entire endo- and exocervix with an irregularly enlarged uterine corpus; abdomen; vulva, vagina, and adnexa appeared normal with negative node-bearing areas. Pathologically, the lesion was diagnosed as a well-differentiated adenocarcinoma and an epidermoid carcinoma *in situ* with a few small leiomyomas in the myometrium.

70-1128 ORAL CONTRACEPTIVES AND CERVICAL CANCER. A PRELIMINARY REPORT OF AN EXPERIMENTAL STUDY. (E.) Myhre, E. (State Hosp., Oslo) and K. Bjørro. Acta Path. Microbiol. Scand. 76(3):495-496, 1969.

The cervixes of more than 400 WLO mice were painted with 7,12-dimethylbenzanthracene (DMBA; 1% soln., 1 painting/week throughout the observation period). Pellets containing 40% active hormone and 60% cholesterol were implanted s.c. In animals observed for 30 weeks, cervical carcinoma developed in 18/19 controls painted with DMBA only; in all animals that were oophorectomized (oos.; 11 mice) or admin. chlormadinone acetate (5 mg; 19 mice); in 20/22 admin. quingestanol acetate (2.5 mg); in 16/19 admin. norethisterone (5 mg) in 9/18 admin. progesterone (25 mg) and in 6/19 admin. testosterone propionate (10 mg). The incidence of carcinoma in controls, in oos. animals and in mice admin. chlormadinone, observed for about 15 weeks, was 1/41, 1/11 and 1/22, resp. No carcinomas developed in any of the other groups. Ethynylestradiol (1.25-5 mg) induced cervical carcinomas in 12/24 mice surviving more than 5 weeks (av. 9.3 weeks).

70-1129 PITUITARY TUMORS IN MICE INJECTED WITH DELESTROGEN. (E.) Ydrach, A. A. (U. Puerto Rico Sch. Med., San Juan). Bol. Asoc. Med. P. Rico 61(7):236-243, 1969.

Estradiol valerate (Delestrogen; 10 µg every 2 weeks s.c.) was admin. to 68 C57BL mice. In females sacrificed in 8-12 mo., the ovaries had no mature follicles or corpora lutea; all mice had been in permanent anestrus, and none reproduced. The testes of the males were half normal

size, with no mature spermatozoa. Examination of the pituitaries from 30-477 days showed a decrease in the acidophilic cells by more than 25%; the basophilic cells were only slightly reduced. Pituitary tumors were found in 19/62 (9 in the anterior lobe, 6 in the intermediate lobe and 4 of unknown site of origin). The histology of these tumors is described. In addition, 6/62 mice developed lymphosarcoma, 1 had a lung tumor and many females had pyometria. Among the 65 controls, none developed pituitary tumors, 3 developed lymphosarcomas, 2 showed lung tumors and 1 developed a hepatoma.

70-1130 AUTONOMOUS VARIANTS OF AN ANDROGEN/
ESTROGEN-INDUCED AND -DEPENDENT DUCTUS
DEFERENS LEIOMYOSARCOMA OF THE SYRIAN HAMSTER.
(W.) Kirkman, H. (Stanford U. Sch. Med., Calif.)
and F. T. Algard. Cancer Res. 30(1):35-40, 1970.

Transplantation of leiomyosarcomas, of the epididymis and ductus deferens, induced in male Syrian hamsters by subpannicular implantation of 30 mg pellets of testosterone and diethylstilbestrol and 20 mg pellets of estradiol, was successful only in estrogen/androgen treated hosts. In 2 males carrying palpable tumors of the 1750 line (67 passages), hormone treatment was discontinued after 54 days and the tumors regressed for 2 mo., then reappeared. From these 2 tumors, 1 hormonally-independent line developed (with a mean latent period of 8 days), which grew equally well in males and females. Another autonomous tumor line was developed from line 7397 by a similar withdrawal of hormone. Autonomous tumors could not be selected by storage in liquid nitrogen and *in vivo-in vitro* cultivation. The histology of these tumors is described.

70-1131 ENDOCRINE GLAND TUMORS AND METABOLIC
DISTURBANCES OF PORPHYRINS INDUCED BY
LONG TERM FEEDING OF LEAD ACETATE TO RATS. (Pol.)
Medraś, K. (Med. Acad. Inst. Anat. Path., Breslau,
Poland) and B. Zawirska. Pat. Pol. Suppl.
1:49-51, 1969.

Feeding lead acetate to 126 Wistar rats for 18 mo. (total dose 2130 mg/rat; no other details) resulted in a high incidence of benign and malignant endocrine tumors in animals of both sexes (adenoma of the pituitary or thyroid in 3.9% and 3.1%, resp.; carcinoma of the thyroid in 0.8%, adenoma and carcinoma of the adrenals in 23.2% and 0.8%, resp.). Other tumors developing in males were interstitial metaplasia of the testis (57.4%), interstitial cell tumors of the testis (24.4%), and adenoma or carcinoma of the prostate (22.3% and 1.0%, resp.). Females also developed follicular cysts and hyperplasia of theca granulosae (25%) and interstitial hyperplasia of the ovary (50%). Malignant tumors of both testes or both adrenals and other organs occurred frequently in the same animal. After

19-24 mo., irreversible disturbances of porphyrin metabolism were indicated by a marked increase in coproporphyrin and 8-carboxyporphyrin excretion. The amount of porphyrins in the tissues of experimental rats was much larger than in controls; the greatest amounts were found in the bone marrow (mostly protoporphyrin) and kidneys (mostly uroporphyrins). Disturbances in porphyrin metabolism and kidney damage preceded the neoplastic changes. The severe disturbances in hormonal homeostasis were regarded as co-carcinogenic factors.

70-1132 INCIDENCE OF TUMORS AFTER IMPLANTATION
OF PLASTIC MATERIALS. (Pol.) Kawecki,
K. (Med. Acad. Breslau, Poland). Pat. Pol.
Suppl. 1:593-595, 1969.

Early and late tissue reactions to plastic materials of different shape, size, surface and porosity (implanted s.c. or i.p.) was studied in 3 series of experiments using a total of 1440 Wistar rats (3-9-mo. old, both sexes). The early reaction (590 rats; 1-90 days after implantation) to solid discs of polyamide, polyester, polyethylene and polypropylene, in contrast to the reaction to nets of the same materials, was characterized by poor vascularization of the granulation tissue and scanty (11 foreign body giant cells (possibly macrophages). Long-term experiments (24-28 mo.) on 850 rats revealed a 84-100% incidence of tumors in animals implanted with solid discs, compared to 63-65% in those implanted with perforated discs of the same size, 5.3% in those implanted with coils of polyamide strands, and 5% in those implanted with 5 layered discs of #11 polyester; no tumors were induced by single layer discs of polyester net #11 or #3 (surface 2 cm²). Differences in late tissue reactions to solid discs and nets were observed and described. Tumors also developed in 31/120 rats surviving 12 mo. after implantation of solid discs of epoxy resins. The induced tumors (latent period of 10-18 mo.) were malignant sarcomas, frequently with lung metastases, and could be transplanted into animals of the same strain (no other details). It is concluded that the oncogenicity of plastic materials is dependent on their physical shape and the amount implanted, and that the tumor incidence is reduced when large numbers of "foreign body giant cells" persist in the tissue surrounding the implant.

70-1133 OSTEOGENIC SARCOMA IN RABBITS FOLLOWING
SUBPERIOSTEAL IMPLANTATION OF
BERYLLIUM. (E.) Tapp, E. (Withington Hosp.,
Manchester, England). Arch. Path. (Chicago)
88(1):89-95, 1969.

Zinc beryllium silicate, beryllium oxide, or beryllium silicate (10 mg in each case) was implanted subperiosteally in the upper right

bia of 18 rabbits of mixed breeds and sexes (6-8 weeks old). Typical central osteogenic sarcomas developed in 4 animals between 10-25 mo., but 8 had been killed between 10-18 mo. with X-ray signs suggesting a tumor. The tumors were of the juxtacortical type, but arose from the medullary cavity and extended outwards through the cortex into the soft tissues. This was thought to be due to rapid incorporation of the beryllium salt into the medullary cavity. Lung metastases were seen in 3/4 animals.

0-1134 MORPHOGENESIS OF BERYLLIUM-INDUCED BONE TUMORS. (Pol.) Komitowski, D. Aleja Niepodleglosci 142, Warsaw). Pat. Pol. suppl. 1:479-482, 1969.

1% suspension of beryllium oxide was inj. i. v. into 30 rabbits (total dose in 20 rabbits 1 g, in 10 less than 1 g). Three phases of berylliosis were differentiated: initial (toxic effect), fibrosis and carcinogenic. Fibrosis was most pronounced in lungs, spleen and liver. Fibrosis of bone marrow was considered as the precancerous stage. Osteogenic sarcomas (2 in forelegs, 1 in spine) were detected in 3 animals surviving more than 15 mo. In two animals, numerous metastases to lungs were also observed. All 3 tumors were characterized by an extremely high level of alkaline phosphatase activity. Serum alkaline phosphatase activity was elevated (av. 20 Bodansky units) while enzyme activity in liver and kidneys was reduced. Histologically the cells of all tumors showed a tendency to differentiate into atypical osteoblasts, indicating a histogenetic connection with young connective tissue elements of the bone marrow which are capable of differentiation into osteoblasts. It is concluded that neoplasia resulting from beryllium intoxication is the last phase in a series of cyclic changes taking place in different tissues; the most essential of these is fibrosis.

-1135 CADMIUM AND ZINC ABNORMALITIES IN BRONCHOGENIC CARCINOMA. (E.) Morgan, M. (U. Alabama Sch. Med., Birmingham). Cancer (6):1394-1398, 1970.

Serum and tissue conc. of cadmium and zinc were measured in 3 groups of pts.: 47 men (av. age 60) with bronchogenic carcinoma and no other neoplasms; 50 men (av. age 60) with a variety of neoplastic disease; and 55 controls (av. age 61; 26 women, 54 men) with no chronic renal or hepatic disease, neoplasms or obstructive lung disease. The hepatic, renal and serum cadmium conc. was significantly higher in pts. with bronchogenic carcinoma than in controls; no significant difference in the cadmium levels was seen between controls and the group with varied neoplastic diseases. Tissue zinc conc. was only slightly above control values in both cancer groups, and the hepatic levels were not

significantly different, but serum zinc levels were distinctly lower in the group with bronchogenic carcinoma.

70-1136 ESTROGEN METABOLISM IN PATIENTS AT HIGH RISK FOR ENDOMETRIAL CARCINOMA.

I. URINARY METABOLITES OF H^3 -ESTRADIOL IN NORMAL POSTMENOPAUSAL WOMEN AND THOSE WITH ENDOMETRIAL CARCINOMA. (E.) Hausknecht, R. U. (Mount Sinai Sch. Med., New York, N. Y.) and S. B. Gusberg. Amer. J. Obstet. Gynec. 105(8): 1161-1167, 1969.

Urine samples (96-hr. samples) were collected after i.v. infusion of 3H -estradiol (8 μ c/10 ml of 10% propylene glycol) from 51 women (including 34 with endometrial carcinoma). After hydrolysis with β -glucuronidase, the free steroids were chromatographed and the radioactivity of each peak measured. No significant difference was seen in the urinary levels of estrone, estradiol and estriol, or in the "estriol quotient" (estriol/estrone + estradiol), between pts. with carcinoma and the others, but estriol had a relatively lower specific activity in both groups.

70-1137 EFFECT OF BASIC CUPRIC ACETATE ON THE BIOCHEMICAL CHANGES IN THE LIVER OF THE RAT FED CARCINOGENIC AMINOAZO DYE. I. CHANGES IN THE ACTIVITIES OF DAB METABOLISM BY LIVER HOMOGENATE. (E.) Yamane, Y. (U. Chiba, Japan), K. Sakai, I. Uchiyama, M. Tabata, N. Taga and A. Hanaki. Chem. Pharm. Bull. (Tokyo) 17(12):2488-2493, 1969.

Groups of 40 female 100-150 g Wistar rats were fed 4-dimethylaminoazobenzene (DAB; 0.09%) and/or basic cupric hexahydrate (0.5%) in a maize diet ad libitum (5 days/week). The increase in body wt. was slow for all groups, and rats fed DAB alone had enlarged spleens and liver nodules by week 20. Rats admin. copper showed an increase in the copper content of the liver; and the metabolism of DAB was enhanced, as noted by the decreased content of DAB and a metabolite, 4-methylaminoazobenzene. Azo-reduction activity was enhanced in the liver of copper-fed rats, reaching a max. triple that of controls in about 2 weeks; the N-demethylase activity was high in rats fed DAB and was significantly reduced by copper feeding; the aromatic hydroxylase activity was unaffected by DAB or copper.

70-1138 CHANGES IN CARBOHYDRATE METABOLISM IN THE LIVER DURING CARCINOGENESIS BY DIMETHYLAMINOAZOBENZENE. III. STUDIES OF THE METABOLISM OF THE PENTOSE PHOSPHATES. (Fr.) Jacob, A. (Cancer Res. Ctr., Villejuif, France). Int. J. Cancer 5(1):111-118, 1970.

In homogenates of normal, precancerous and cancerous rat liver, glucose-6-phosphate (G6P)

dehydrogenase activity increased and 6-phosphogluconate (6PG) dehydrogenase activity decreased progressively throughout the course of *in vivo* 4-dimethylaminoazobenzene (DAB) carcinogenesis. The suggested decrease in rate of transformation of 6PG into ribulose-5-phosphate (R5P) was confirmed by studies of the disappearance rate of 6PG when the 3 types of tissue were incubated with the same substrate for 2 hours. The total quantity of hexose phosphates formed by the end of 2 hours was reduced (by as much as 50%) in incubations with precancerous or cancerous tissue, with no additional hexose phosphates appearing after 30 min. (although 6PG continued to disappear), despite the fact that hexose phosphate formation continued uninterrupted throughout the incubation period in the presence of normal tissue. Since the metabolism of R5P *in vitro* was virtually completed by the end of 10 min. (for all 3 types of tissue substantially identical quantities of hexose phosphates were formed during the first 30 min.), the failure of hexose phosphates to increase thereafter, despite the continued disappearance of 6PG, was attributed to diminished isomerase activity which transformed R5P into ribose-5-phosphate, thus diminishing the relative quantity of ribose-5-phosphate in relation to the xylulose-5-phosphate which resulted from epimerase activity. The 6PG which was not transformed into R5P was metabolized, rather than retained, by the cancerous and precancerous tissues, although the metabolic pathways were not clear. However, a part of it definitely entered a shunt pathway which precluded its return by the Embden-Meyerhof pathway, accounting, at least to some degree, for the hypoglycemia observed in rats undergoing carcinogenesis with DAB.

70-1139 EFFECT OF RIBOFLAVIN ON PHOSPHOLIPID OF THE RAT LIVER DURING DAB HEPATO-CARCINOGENESIS WITH SPECIAL REFERENCE TO THE STRUCTURAL ANALYSIS WITH INFRA-RED ABSORPTION SPECTRA. (E.) Hanada, M. (Hirosaki U. Sch. Med., Japan). *Hirosaki Med. J.* 21(2):307-308, 1969.

The livers of male albino rats fed a normal diet, especially with vitamin B₂ added, had a slightly higher phospholipid level (PL) than rats fed 4-dimethylaminoazobenzene (DAB). A low PL level was seen in rats given a normal diet with mitomycin C (MC) added, or rats in which ascites hepatoma (AH 130) was transplanted, and a very low level in rats with ascites tumor fed MC alone or + strong Neo-Minophagen C (SNMC) combined. Thin-layer chromatography indicated a relative increase in the lecithin and cephalin content in groups fed DAB, large amounts of flavin adenine dinucleotide or flavin mononucleotide. All PL increased equally with MC, AH 130 or a combination of AH 130, MC, and SNMC. Sphingolipid, lecithin and cephalin increased when AH 130 and MC were admin. together.

70-1140 ESTABLISHMENT OF NEW ASCITES HEPATOMAS. (E.) Kimoto, K. (Okayama U. Med. Sch. Cancer Inst., Japan). *Acta Med. Okayama* 23(1): 27-46, 1969.

Different strains of rat hepatomas were induced by providing Donryu rats with a diet containing 4-dimethylaminoazobenzene (DAB; 0.06%) for various lengths of time (longer than 191 days), transplanted to the brain of newborn Donryu rats, and converted to an ascites tumor by inoc. of tumor cells i.p. into adult Donryu rats. Four strains of ascites tumors could be differentiated by the gross appearance of the nodules they produced. Transplantability was 92-98%, with little or no change in increasing transplantation generations. The survival of the rats was inversely related to the length of DAB feeding. Histologically, the different strains resembled their parent tumor, the tumors induced by longer feedings being more anaplastic. The number and distribution of chromosomes were markedly different between strains.

70-1141 FRACTIONATION OF NUCLEI FROM INDUCED HEPATOMAS BY SUCROSE GRADIENT CENTRIFUGATION. (E.) Albrecht, C. (Nat. Chem. Res. Lab., Pretoria, South Africa). *Exp. Cell Res.* 56(1): 44-48, 1969.

Hepatomas were induced in 2/8 male and 2/4 female rats fed a diet of 3'-methyl-4-dimethylaminoazobenzene (0.6372 g in 24 ml olive oil/100 g stock diet for 3 mo.). The tumors were homogenized by a modified process which released over 90% of the nuclei, rupturing few large ones. The nuclei were free of cytoplasmic tags. The homogenate was then centrifuged in a 1.0 M linear sucrose gradient and the nuclei separated into 3 main zones (A, B and C). Zone A contained the diploid parenchymal and stromal nuclei, zone B the tetraploid nuclei, and zone C those nuclei larger than tetraploid. In comparison to control liver tissue and tissue adjacent to the tumor, nuclei from the tumor showed a diploid zone with a relative reduction in density, no clear demarcation between the tetraploid and C zones, and some nuclei which penetrated further along the gradient.

70-1142 DEOXYCYTIDYLATE DEAMINASE AND RELATED ENZYMES OF THYMIDINE TRIPHOSPHATE METABOLISM IN HEPATOMAS AND PRECANCEROUS RAT LIVER. (E.) Sneider, T. W. (U. Wisconsin Med. Sch. McArdle Lab., Madison) and V. R. Potter. *Advances Enzyme Regulat.* 7:375-394, 1969.

Male Holtzman rats (200-225 g) were fed 3'-methyl-4-demethylaminoazobenzene (3'-MDAB; 0.06%) ad libitum or 3'-MDAB (0.05%) from 9 a.m. to 5 p.m. Rats were killed at weekly intervals and livers homogenized in 0.5 mM deoxycytidine triphosphate

assayed by radioisotope labeling and chromatographic separation for certain enzymatic levels of thymidine triphosphate metabolism. No significant elevation of deoxythymidine monophosphate synthetase was observed in rats fed dye for a period of 17 weeks. The ability of the liver to degrade thymidine to CO₂ was 75% that of control levels in dye-fed rats after 1-2 weeks, but by week 4 returned to high adult levels. The deoxycytidine monophosphate deaminase and thymidine kinase levels were elevated after 2 weeks, but fell to low adult levels at 8 weeks.

1143 CHANGES IN THE NUCLEOTIDE COMPOSITIONS OF NUCLEOLAR 45 S RNA OF AZO DYE-INDUCED HEPATOMA. (E.) Matsuhisa, T. (Osaka U. Med. Sch. Inst. Cancer Res., Japan), K. Higashi, T. Gotoh and Y. Sakamoto. Cancer Res. 30(1):12-166, 1970.

Sprague-Dawley rats (about 100 g) were fed diets containing 3'- or 4'-methyl-4-dimethylamino-2-benzene (MDAB; 0.06%). No significant difference was observed in the sucrose density gradient sedimentation patterns of nuclear RNA from rats fed a normal diet or those fed 3'- or 4'-MDAB. The nucleotide content of total nuclear RNA from tumor-free rats fed 3'-MDAB for 3-6 months was also similar to that of controls, although histological changes were seen. However, the purinic acid content in the 45S RNA from 3'-MDAB-induced hepatomas was lower, and the nucleotide content of the total RNA differed from that of controls. Base composition of nucleolar 28S RNA from tumor tissue had the same difference from normal as the 45S RNA.

1144 METHYLATION OF TRANSFER RNA AND OF RIBOSOMAL RNA IN RAT LIVER IN THE INTACT ANIMAL AND THE EFFECT OF CARCINOGENS. (E.) Craddock, V. M. (Med. Res. Council Labs., Chesham, Surrey, England). Biochim. Biophys. Acta 195(2):351-369, 1969.

Male Wistar albino rats (of the Porton strain) were admin. dimethylnitrosamine (DMNA) in the diet (50 ppm x 7.5 or 23 weeks), inj. i.p. with DMNA (30 mg/kg), fed 20% Rosetti Brazilian peanut meal with aflatoxins (10 ppm x 50 weeks), or acin. ethionine (0.8% for 4 weeks and 0.6% for 2 weeks), then inj. with ¹⁴C-methionine (50 µCi i.p.), sacrificed, and the nucleic acid of the liver and intestine analyzed. Incorporation of ¹⁴C-methionine into the liver and intestinal protein was the same for treated and control animals, while increased labeling was seen for each of the methylated bases of transfer RNA (each base increased to a different extent in the liver and to the same extent in the intestine) in all animals treated with carcinogen. This was attributed to a shift in the different species of transfer RNA synthesized during carcinogenesis. The increase in labeling of methylated bases in ribosomal RNA was correlated with an increased synthesis of ribosomal RNA.

70-1145 EFFECTS OF THE PERORAL ADMINISTRATION OF DIMETHYLNITROSAMINE IN ADULT RATS. (It.) Palestro, G. (U. Turin Inst. Anat. Histopath., Italy) and M. L. Codegone. Pathologica 60(889-890):395-399, 1968.

Adult rats receiving dimethylnitrosamine p.o. in drinking water (0.01% soln. x 8 days) developed 3 renal and 1 hepatic tumor among 5/18 which survived to sacrifice on days 43-59. The remaining 13/18 died after 2-8 weeks, as did 8/15 receiving a 0.005% soln. x 14 days. Renal tumors were found in 4/7 survivors at the time of sacrifice as above. No renal or hepatic tumors developed among 10/10 which survived treatment with a 0.0025% soln. x 14 days. However, when treatment at this dose level was extended to 56 days, 1/19 failed to survive the treatment period and 15/18 survivors had developed hepatic tumors by the time of sacrifice. Renal tumors were primarily adenomas, with a few nephroblastomas. Hepatic tumors were adenocarcinomas or trabecular and anaplastic carcinomas.

70-1146 INVESTIGATION OF THE ALKYLATING ACTION OF 1,1-DIMETHYLHYDRAZINE. (E.) Krüger, F. W. (German Cancer Res. Ctr. Inst. Exp. Toxicol. Chemother., Heidelberg), M. Wiessler and U. Rucker. Biochem. Pharmacol. 19(5):1825, 1970.

Male Sprague-Dawley rats (300-350 g), with solid-growing Yoshida transplantation tumors (2-3 g), were inj. with ¹⁴C-1,1-dimethylhydrazine hydrochloride (80 mg/45 µCi/kg i.v.). After 6 hr., the RNA of the liver showed little radioactivity (incorporation of label into the purine bases), while the RNA of the tumor was labeled. No 7-methylguanine was seen. It is concluded that this compound is not considered to be an alkylating intermediate, although it may be formed from dimethylnitrosamine.

70-1147 DIETHYLNITROSAMINE ONCOGENESIS IN RF MICE AS INFLUENCED BY VARIATIONS IN CUMULATIVE DOSE. (E.) Clapp, N. K. (Oak Ridge Nat. Lab., Tenn.), A. W. Craig and R. E. Toya, Sr. Int. J. Cancer 5(1):119-123, 1970.

Diethylnitrosamine (DEN) was admin. to 8-10-week-old male RF mice in drinking water (2-11.5 mg/kg/day) for varying periods; cumulative doses ranged from 57-943 mg/kg body wt. In all treated groups, incidences of lung adenomas, hepatomas and forestomach squamous cell carcinomas exceeded those in controls; max. incidences reached 84%, 98% and 100%, resp., compared to control values of 41%, 5% and 0%, resp. At lower doses, incidence of liver tumors increased linearly with the dose, reaching 80-90% at DEN doses of 300 mg/kg and above, but the lowest dose of DEN induced a max. incidence of lung tumors. Only at the lowest dose did DEN fail to induce a max. incidence of stomach tumors. The

mean survival time, mean age at death with all types of tumors, and minimum induction times decreased with increasing dose. DEN did not exert a leukemogenic effect at the doses used, and an inhibitory effect was suggested; only 1/371 (0.3%) DEN-treated mice developed myeloid leukemia and 4/371 (1%) thymic lymphoma, compared to control values of 7/162 (4%) and 6/162 (3.7%), resp. At the lowest dose used, the lung appeared to be most sensitive (max. tumor induction), the stomach intermediate in sensitivity and the liver least sensitive to DEN-oncogenesis.

70-1148 STUDIES ON FRUCTOSE PHOSPHATE ALDOLASE DURING EXPERIMENTAL LIVER DAMAGE IN RATS. II. LIVER DAMAGE BY DIETHYLNITROSAMINE. (Ger.) Dikow, A. L. (Boul. Christo Botew 14, Sofia, Bulgaria) and D. C. Hadjiolov. Z. Klin. Chem. 7(5):556-558, 1969.

Male albino rats (140-160 g) were admin. diethylnitrosamine (DENA; 1 mg/day, 6 admin./week in drinking water) and sacrificed 30 and 60 days later. Histochemical examination of the livers revealed chromatolysis first in the region of central lobes and, after 60 days, diffused throughout the parenchyma. A large number of hepatocytes showed "vacuolar degeneration" and the cytoplasm showed large granular deposits of diformazan. The total aldolase activity in the serum doubled (from 56.46 mU/ml to 106.92 and 112.59 after 30 and 60 days, resp.). This was accompanied by an increase in intensity and number of isoenzyme fractions in the serum. The electrophoretic mobility of the changed serum isoenzyme pattern corresponded to the mobility of type B aldolase fractions from normal liver. Total liver aldolase activity decreased (fructose 1,6- diphosphate (FDP) from 0.93 μ Mol/mg tissue protein/minute to 0.36 after 60 days and fructose-1-phosphate (FMP) from 0.83 to 0.24), while the FDP/FMP ratio increased from 1.12 to 1.50. It is concluded that DENA (contrary to some reports) causes extensive necrobiotic changes in the liver parenchyma during the early stages of carcinogenesis.

70-1149 CRITICAL TIME DEPENDENCY OF THE EFFECT OF LIVER REGENERATION ON CARCINOGENESIS IN RAT LIVER. (Ger.) Hoffmann, M. (Max Planck Inst. Virol., Tübingen, Germany). Z. Naturforsch. [B] 25b(4):434-435, 1970.

Diethylnitrosamine (DENA; 6 mg/kg x 6 weeks) was admin. p.o. to groups of female Sprague-Dawley rats; partial hepatectomy was performed either at the start of the experiment or at 1 week intervals for 4 weeks. Examination of the livers 6 weeks after discontinuation of DENA feeding revealed that the number and areas of "islands" devoid of glucpse-6-phosphatase activity was significantly increased in animals which underwent hepatectomy during the weeks 1-2 of feeding, slightly increased in those hepatectomized

after 3 weeks, but was the same as in control animals when hepatectomy was performed after 4 weeks of feeding. Examination of similarly treated animals 12 mo. after start of experiment showed that while 0/6 control animals (no hepatectomy) had tumors greater than 10 mm in diameter, 1/5 hepatectomized immediately and 4/4 hepatectomized after 2 weeks of feeding had tumors greater than 10 mm in size. Tumors were also more numerous, weight of livers greater and areas (%) devoid of glucose-6-phosphatase activity larger in hepatectomized animals. It is concluded that liver regeneration has a carcinogenesis-supporting effect when it occurs during the first 3 weeks of DENA admin.

70-1150 EFFECTS OF NITROSOMETHYLUREA AND NITROSOMETHYLURETHAN ON THE PHYSICAL CHEMICAL PROPERTIES OF DNA. (E.) Rosenkranz, H. S. (Columbia U. Coll. Physicians Surg., New York, N. Y.), S. Rosenkranz and R. M. Schmidt. Biochim. Biophys. Acta 195(1):262-265, 1969.

Purified ^3H -DNA (100 $\mu\text{g/ml}$), incubated with 0.02 M methylnitrosourea or methylnitrosourethan, was not degraded to acid-soluble products, as was DNA contained in bacterial cells. The sedimentation coefficient of the polydeoxynucleotide molecule decreased; breaks in the DNA backbone were seen when the twin helices were separated by formamide. The reactions between DNA and the drugs were a function of time, temperature and conc., which reflected both the direct action of the agents on DNA and the rate of spontaneous decomposition of the agents. The denaturation of DNA as a result of direct alkylation is discussed.

70-1151 INTERACTION OF N-METHYL-N'-NITRO-N-NITROGUANIDINE WITH ASCITES HEPATOMA CELLS IN VITRO. (E.) Nagao, M. (Nat. Cancer Ctr. Res. Inst., Tokyo), T. Yokoshima, H. Hosoi and T. Sugimura. Biochim. Biophys. Acta 192(2):191-199, 1969.

Ascites hepatoma cells (AH 7974) from Donryu rats incorporated in vitro about 2 times more ^{14}C -guanidino-N-methyl-N'-nitro-N-nitrosoguanidine (NG) than ^{14}C -methyl-NG. The radioactivity incorporated after 10 min. was not released by the cells, or converted to an acid-soluble form after the cells were resuspended in Krebs-Ringer phosphate buffer. Labelled histone was separated from the deoxyribonucleoprotein of cells treated with ^{14}C -guanidino- or ^{14}C -methyl-NG and hydrolysis and paper chromatography of the histones in the former case showed all the radioactivity in the area coinciding with L-nitrohomoarginine. Radioactivity was observed in DNA and ribosomal and transfer RNA only in cells incubated with ^{14}C -methyl-NG.

70-1152 TRANSPLACENTAL CARCINOGENESIS IN MICE BY 1-ETHYL-1-NITROUREA. (E.)

ce, J. M. (NIH, Bethesda, Md.). Ann. NY Acad.
163(2):813-826, 1969.

enatal inj. of 1-ethyl-1-nitrosourea (0.25-1.0
/kg i.p.) induced lung tumors in young NIH
eral Purpose mice when given to their mothers
early as day 12 of gestation. The tumors
re histologically similar to those induced in
ult mice and were dose-dependent at every
stational stage. A dose which was negligibly
cincogenic in pregnant adults (0.25 mmole/kg)
adily induced lung tumors in their progeny if
ven at a time of max. sensitivity (14 tumors/
se treated at day 16 of gestation). Data
om other strains (e.g. A/J and C57Bl/6N)
onstrated a similar max. sensitivity about
5 days prior to parturition.

1153 EXPERIMENTAL BRAIN TUMOURS IN DOGS.
(E.) Warzok, R. (Med. Acad. Path.
st. Erfurt, Germany), J. Schneider, D. Schreiber
l W. Jänisch. Experientia 26(3):303-304, 1970.

mongrel dogs (aged 4 mo. to 3 yr.; 6 male, 4
ale) received 1-methyl-1-nitrosourea (MNU; 20
/kg/mo. i.v.; total absolute dose, 1.0-4.274 g).
ir animals (3 male, 1 female) developed brain
ors histologically resembling intracerebral
comas or glioblastoma multiforme; all tumors
wed signs of malignancy. In 4 dogs, other
ans developed multiple separate tumors, which
e sarcomas and malignant hemangioendotheliomas,
ilar to tumors obtained with MNU in rabbits.
se tumors were considered to be an expression
a systemic neoplastic process and not
astases from a single blastomatous focus.

1154 ADENOCARCINOMAS OF THE INTESTINE
INDUCED IN SYRIAN HAMSTERS BY N-METHYL-
ITROSOUREA. (E.) Herrold, K. M. (NCI,
hesda, Md.). Path. Vet. (Basel) 6(5):403-412,
9.

ian hamsters (1 mo. old), inj. i.v. with N-
hyl-N-nitrosourea (NMU; 2.5 mg/mo. x 3-4 mo.)
an av. lifespan of 9 mo.; animals inj. i.p.
NMU (1 mg/week x 4-5 mo.) had an av. life-
n of 11 mo.; and animals treated p.o. with
(1 mg; 2 doses/week x 4 mo.) had an av. age
death of 9 mo. (the av. life-span of untreated
ontrols was 19.5 mo.). The adenocarcinomas
uced in the intestine were classified as 2
ys, superficial and intestinal, and the
iology described. The experimental animals
eveloped intestinal neoplasms as early as 6 mo.,
eared to 12 mo. in the controls; adeno-
inomas of both small and large intestines
e seen in 5 animals inj. i.v. and in 2 inj.
Animals inj. i.v. had the highest frequency
metastases.

1155 DIFFERENCES IN THE ACTION OF NITROSO-
METHYLUREA AND STREPTOZOTOCIN. (E.)

Rosenkranz, H. S. (Columbia U. Coll. Physicians
Surg., New York, N. Y.) and H. W. Carr. Cancer
Res. 30(1):112-117, 1970.

Escherichia coli were treated with methylnitroso-
urea (MNU; 0.005-0.01 M) methylnitrosourea
(, MUN) or streptozotocin (S; a 2-deoxy-D-glucose
derivative of MNU). The bactericidal action of
S was much lower than that of MNU or MUN in
corresponding conc. The amounts needed to
inhibit DNA synthesis were similar for the 3
compounds, but S had much less effect on RNA and
protein synthesis than MNU or MUN. Cellular
devitalization induced by MNU and MUN was
blocked by inhibitors of energy metabolism
(sodium azide or dinitrophenol), which had no
beneficial effect on S-treated bacteria. No
cross-resistance was observed between bacteria
resistant to MNU and MUN, and S-resistant
bacteria; marked differences were seen between
these strains in the basis of their resistance.
A different metabolic effect of the agents on
Ehrlich ascites carcinoma cells was also noted.

70-1156 EXPERIMENTAL STUDIES ON URINARY BLADDER
TUMORS: I. ON THE DEVELOPMENT OF
URINARY BLADDER TUMOR IN RATS INDUCED BY N-BUTYL-
N-BUTANOL (4) NITROSAMINE. (Jap.) Ishikawa, M.
(Nara Med. U., Kashihara, Japan), E. Okajima,
T. Imoto, T. Hiramatsu, N. Ito, Y. Konishi and
Y. Hiasa. (Jap. J. Urol.) Nippon Hinyokika
Gakai Zasshi 60(2):99-108, 1969.

Admin. of N-butyl-N-butanol (4)-nitrosamine
(BBN; 0.05%, av. 11.5 ± 1.2 mg/day x 24 weeks
p.o.) to male Wistar rats induced urinary bladder
tumors (transitional cell type, resembling human
bladder tumors) in 10/10; renal pelvic tumors
were also seen in 2/10. BBN exhibited an
organotropic effect on the epithelium of the
urinary tract, especially the bladder, with a
high incidence rate and short induction time.
The bladder tumors showed high histochemical
activities of monoamine oxidase (3+), acid
phosphatase (2+) and β -glucuronidase (3+).

70-1157 METHYLATION OF RAT-LIVER RNA IN VIVO
BY METHYL METHANESULPHONATE. (E.)
Whittle, E. D. (U. Edinburgh Med. Sch.).
Biochim. Biophys. Acta 195(2):381-388, 1969.

Purified liver RNA from 9 male albino rats, inj.
with ^{14}C -methyl methanesulfonate ($98 \mu\text{C} + 15$
mg/l ml saline soln. i.p.), was acid-hydrolyzed
and separated by ion-exchange chromatography.
After 1 hr., 73% of the radioactivity appeared
as a single peak corresponding to 7-methyl-
guanine (7-MG). Since no radioactivity corre-
sponding to the guanine absorbance peak was
found, this was probably the result of direct
in vivo methylation. The level of 7-MG at this
time was 80% of max. and remained at near max.
from 2-24 hours. At 4 hours after inj., ring
labeling of guanine and alanine began to appear;

by 24 hours, incorporation of radioactivity into RNA by normal biosynthetic pathways accounted for more than 80% of the total RNA label.

- 70-1158 MUTAGENICITY OF ALKYLATING CARCINOGENS. (E.) Malling, H. V. (Oak Ridge Nat. Lab., Tenn.) and F. J. de Serres. Ann. NY Acad. Sci. 163(2):788-800, 1969.

The mutagenic activity of methyl methanesulfonate (MMS) and N-methyl-N'-nitro-N-nitrosoguanidine (MNNG) was characterized with regard to genetic alterations, using the ad-3 test system of *Neurospora*. Treatment with MNNG (25 μ M x 60 or 120 min.) led to 0.5 and 1% chromosome deletions among 238×10^{-6} and 592×10^{-6} ad-3 mutations/survivor, resp.; MMS (20 μ M) produced 15.7% chromosome deletions among 367×10^{-6} ad-3 mutations. The MNNG-induced mutants had 81% non-polarized complementation patterns, compared to 37% of the MMS-induced mutants. The intragenetic alterations induced by MNNG, a strong carcinogen, gave rise to gene products with altered function, whereas MMS, a weak carcinogen, induced abnormalities which led to inactive gene products.

- 70-1159 THE ALLEGED ONCOGENIC ACTIVITY OF ISONIAZID. (It.) Zorini, A. O. (U. Rome Hist. Clin.). Rass. Clin.-Sci. Ist. Biochim. Ital. 45(1):1-4, 1969.

Incubation of isoniazid (INH) with human amniotic cells *in vitro* in conc. up to 3 mg/ml failed to inhibit cellular replication, and no other evidence of a cytostatic effect was seen. Spectrophotometric studies confirmed that INH was metabolized fairly rapidly into acetyl-INH. In contrast to cultures of mouse lung cells, cultures of human lung cells incubated with INH metabolized significantly more of the compound into acetyl-INH, with a corresponding reduction of the formation of isonicotinic acid and/or hydrazine. The amount of hydrazine liberated in reported studies of INH in mice was estimated as 30 times greater than that liberated by therapeutic doses in man. Studies in mice, golden hamsters and guinea pigs failed to show any carcinogenic or precarcinogenic effects of INH at doses up to 100 mg/kg/day, although some benign, reactive hyperplasia of the bronchial mucosa was found, accompanied by regenerative phenomena in the alveolar epithelium. A study of 1600 former tubercular pts., who later developed cancer of the lung, breast, genital organs, g.i. tract, nasopharynx and other sites, showed no correlation between previous INH treatment and subsequent development of bronchogenic or other forms of cancer. The absolute incidence of bronchogenic cancer in this group was 14.4%. It is concluded that INH has neither carcinogenic nor antitumor activity.

- 70-1160 INDUCTION OF CARCINOMAS IN THE NASAL CAVITY OF RATS BY DIOXANE. (E.)

Hoch-Ligeti, C. (VA Ctr., Martinsburg, W. Va.), M. F. Argus and J. C. Arcos. Brit. J. Cancer 24(1):164-167, 1970.

Groups of 30 male Charles River CD rats (110-230 g, 2-3 mo. old) were provided with 0.75-1.8% dioxane in the drinking water for 13 mo. Nasal tumors were observed in 1, 1, 2 and 2/6 rats given 0.75%, 1.0%, 1.4% and 1.8% dioxane, resp. The total dose varied from 104-256 g, based on a daily consumption of 36 ml fluid, and the latent period ranged from 329-487 days. All tumors were squamous cell carcinomas arising in the anterior nasal cavity, with marked keratinization and formation of keratin pearls. Hepato-cellular carcinomas also developed in rats receiving a 1.4% and 1.8% soln. of dioxane.

- 70-1161 STUDIES ON THE ONCOGENICITY OF 3-HYDROXYXANTHINE. (E.) Teller, M. N. (Sloan-Kettering Inst. Cancer Res., New York, N. Y.), G. Stohr and H. Dienst. Cancer Res. 30(1):179-183, 1970.

Newborn, suckling (3-day-old) and weanling (4-week-old) Wistar rats, and newborn and weanling ICR/Ha Swiss mice, were inj. with 3-hydroxyxanthine (OHX) in various routes, dosages and schedules. In general, the mice were less susceptible to oncogenesis than the rats; 6/52 weanling mice developed tumors at the site of OHX inj. (7 mg/week x 1-22 weeks s.c.), compared to 13/30 suckling rats. Newborns seemed to be less prone to tumor induction than weanling animals; male rats were more susceptible than females. The latent period of fibromas in female rats inj. with OHX (16.5 mg/week for 22 weeks) varied from 12-18 mo., while fibrosarcomas appeared in 6-10 mo.; the latent period was not affected by sex. At low doses (less than 90% induction of tumors), the tumor incidence was dose-dependent.

- 70-1162 RELATIONSHIP BETWEEN TRYPTOPHAN METABOLISM AND HETEROTOPIC RECURRENCES OF HUMAN URINARY BLADDER TUMORS. (E.) Yoshida, O., R. R. Brown and G. T. Bryan (U. Wisconsin Med. Sch., Madison). Cancer 25(4):773-780, 1970.

Tryptophan metabolism was studied in 24 men and 14 women (ages 31-83, av. 63 yr.), with carcinoma of the urinary bladder. There was a significant difference in the recurrence of bladder cancer within 5 yr. between those with abnormal tryptophan metabolism (18/18) and those without (12/20). No significant difference was observed in the basal excretion levels of kynurenine and summation of excretion of kynurenine, kynurenic acid and acetylkynurenine in the 30 pts. with recurrent cancer and the 8 pts. with no recurrence. However, the 18 pts. with abnormal tryptophan metabolism and recurrences showed significantly higher urinary levels of kynurenine, kynurenic acid, acetylkynurenine, hydroxykynurenine, xanthurenic acid, and

aminohippuric acid, after admin. of L-tryptophan (g p.o.).

1163 EXPERIMENTAL INDUCTION OF MYELOFIBROSIS WITH MYELOID METAPLASIA. (E.)

gano, S. A. P. (Brookdale Hosp. Ctr., Brooklyn, N.Y.), M. S. Tobin and D. M. Spain. Blood (6):851-858, 1969.

ponin (S; 1.2 mg/kg every four days x 3 weeks) s inj. i.v. into male New Zealand white rabbits; controls received saline i.v. There was a uniform decrease in hematocrit of about 2 pts by the end of S treatment. Within 1 day after admin., there was an intense normoblastemia, often as high as 50% of the nucleated count of peripheral blood. The av. splenic wt. of S-treated animals (10 g) considerably exceeded that of controls (1.6 g). Myelofibrosis developed in 12/17 animals (71%), and there was myeloid metaplasia of the liver in 10/17 (59%) and of the spleen in 12/17 (71%). The histologic lesions produced resembled those of agnogenic myelofibrosis with myeloid metaplasia in man.

1164 LYMPHOMA-LIKE LESIONS INDUCED IN THE HAMSTER CHEEK POUCH WITH TOPICAL VITAMIN A PALMITATE. (E.) Levij, I. S. Rothschild Hadassah U. Hosp., Jerusalem) and A. Liack. Path. Microbiol. (Basel) 34(5):288, 1969.

right cheek pouches of 24 male golden Syrian hamsters (1.5-2 mo. old, 55-65 g) were painted with vitamin A palmitate (20% in liquid paraffin; admin./week x 12 weeks). Reddish nodular and plaque-like lesions up to 4 mm in diameter were present in the mucosa of most of the treated pouches. Epithelial hyperplasia and atypia, increased keratinization and mucoid metaplasia were also noted. Dense infiltration of mononuclear cells (mainly lymphocytes and other cells with a large, irregular, hyperchromic or nucleolar nucleus, and a small amount of cytoplasm) was observed in the lamina propria and mucular wall, similar to the lymphoreticular hyperplasia seen in malignant lymphomas.

1165 STUDIES ON CHEMICAL CARCINOGENS. IX. HOMOLYTIC DEGRADATION OF O,O'-DIACETYL-4-HYDROXYAMINOQUINOLINE-1-OXIDE (1-ACETOXY-4-HYDROXYIMINO-1,4-DIHYDROQUINOLINE). (E.) Igarashi, M. (Nat. Cancer Ctr. Res. Inst., Tokyo), Sawazoe and C. Nagata. Chem. Pharm. Bull. (Tokyo) 17(7):1344-1351, 1969.

degradation of O,O'-diacetyl-4-hydroxyaminoquinoline 1-oxide by heating at about 70° C for 2 hours in dioxane, isopropanol, tert-butanol, methanol and aqueous soln., produced an acetoxy-free radical, resulting in the formation of about 1 molar equivalent of acetic acid. The free radical was probably formed by homolytic fission

of the N-O bond of the hydroxyamino group. Electron spin resonance spectroscopy showed no change after replacement of the hydrogens in either acetyl group with deuterium, but showed other hydrogens in the quinoline ring interacting with the unpaired electron. It is suggested that radical formation may be related to tumor induction.

70-1166 CARCINOGENESIS IN TISSUE CULTURE. IX. MALIGNANT TRANSFORMATION OF CULTURED RAT CELLS TREATED WITH 4-NITROQUINOLINE-1-OXIDE. (E.) Namba, M. (Okayama U. Med. Sch. Cancer Inst., Japan), H. Masuji and J. Sato. Jap. J. Exp. Med. 39(3):253-265, 1969.

Sarcomas were induced in young Donryu rats by s.c. transplantation of cells from whole embryo cultures of the same strain exposed intermittently to 4-nitroquinoline-1-oxide (NQO; 10^{-6} M) for more than 130 days. Embryonic lung cells (30 exposures, total 117 hours) induced tumors in all rats within 60 days. After continuous and intermittent treatment with NQO (10^{-7} - 10^{-6} M), liver cells induced tumors in 75% of newborn rats. These tumors were mostly liver cell carcinomas, with some adenocarcinomas and sarcomas. The transformed cultures exhibited more pleomorphic cells, were randomly arranged and had a higher growth rate. Chromosomal analysis of transformed liver cells and whole embryo cells showed a near-diploid number and a marker chromosome. Normal rat liver cells were much more sensitive to NQO conc. above 10^{-7} M, than NQO-transformed cells.

70-1167 INDUCTION OF CELL PROLIFERATION IN THE MOUSE BLADDER BY 4-ETHYLSULFONYLNAPHTHALENE-1-SULFONAMIDE. (E.) Levi, P. E., D. M. Cowen and E. H. Cooper (U. Leeds Sch. Med., England). Cell Tissue Kinet. 2(3):249-262, 1969.

Mice (A x IF) were admin. 4-ethylsulfonylnaphthalene-1-sulfonamide (ENS; 1 mg) by stomach tube, and 19 hours later, were inj. with ^3H -thymidine. Groups of 5 were killed at 1, then 2 hour intervals and their bladders examined; in a second experiment colchicine (1 $\mu\text{g/g}$ body wt.) was inj. 1 hour prior to sacrifice. The proliferative response of the epithelium induced by ENS was not uniform within a single bladder. The DNA distribution pattern 24 hours after treatment indicated that all ploidy levels (but mainly diploid and tetraploid cells initially) were involved in DNA replication. No chromosomal abnormalities were observed. The frequency of labeling was highest in the basal epithelium and at the vesico-urethral junction. Electron microscopic examination showed increased lysosomal activity among the superficial cells and the formation of large vacuoles in the cells beneath.

70-1168 ALTERATION OF NATIVE DNA TRANSCRIPTION BY THE MUTAGEN HYDROXYLAMINE. (E.)

Taylor, A. T. (Duke U., Durham, N. C.), S. B. Crist and O. W. Jones. Cancer Res. 30(1):95-99, 1970.

RNA synthesis using hydroxylamine-treated bacteriophage T7 DNA as a template as compared to untreated T7 DNA was 60% after 5 min., and less than 20% after 20 min. Sedimentation values of the treated DNA at neutral pH were similar to those for controls; the DNA appeared homogeneous, but at alkaline pH showed a marked variation. Greater amounts of RNA polymerase were required to bind the treated DNA on Millipore filters, even after removal of hydroxylamine, but DNA damaged by hydroxylamine prohibited optimal transcription of RNA at any conc. of polymerase. The damage prohibited transcription - not the DNA.

70-1169 STUDIES ON MORPHOLOGICAL PRECURSORS OF THE MOUSE HEPATOMA INDUCED WITH o-AMINOAZOTOLUENE. I. APPROACH TO THE METHODOLOGY. (E.)

Itoh, K. (Aichi Cancer Res. Inst., Nagoya, Japan). Mie Med. J. 18(2):107-122, 1968.

Inbred 40-50-day-old A/Jax mice were inj. with olive oil (0.1 ml) containing o-aminoazotoluene (10 mg, 1 admin./mo. s.c.). In untreated mice, spontaneous tumors of the liver developed in 7/67 males and 1/44 females; in the treated group (6-9 inj.), 3/11 females and 0/9 males developed tumors; and in those receiving 10-13 inj., the incidence was 9/9 females and 1/6 males. Liver cells swelled to various sizes and shapes in the early period after treatment, the irregular size of the cell and the nucleus, accompanied by intranuclear inclusions, being more prominent in the female. The number of inclusion bodies increased as the number of nuclei decreased and the cell became larger. Hyperplastic nodules then appeared before the development of tumor.

70-1170 FATE OF SUBCUTANEOUSLY INJECTED BENZO (rst)PENTAPHENE IN C57BL/6 MICE. (E.)

Kelley, T. F. (Instrumentation Lab., Inc., Lexington, Mass.). Proc. Soc. Exp. Biol. Med. 133(4):1402-1404, 1970.

In male C57BL/6 Jax mice admin. 3,4,9,10-dibenzpyrene-¹⁴C (DBP; 0.1 ml suspension of 500 µg in peanut oil s.c.), radioactivity was noted at 16 sites (adrenal gland, gallbladder, intestine, lung, liver) other than the inj. site in 11/50 animals. About 85% of the DBP was removed from the inj. site, and this was accomplished in 2 stages. First, in association with the trauma of inj., significant quantities could be detected at other body sites; second was a chronic removal, almost complete at 10 weeks. The rate of tumor formation was not related to the amount of DBP remaining at the inj. site.

70-1171 INFECTION WITH Trichosomoides crassicauda AS A FACTOR IN THE

INDUCTION OF BLADDER TUMORS IN RATS FED 2-ACETYLAMINOFLUORENE. (E.) Chapman, W. H. (U. Washington, Seattle). Invest. Urol. 7(2): 154-159, 1969.

Griedl, Long-Evans, and Fischer rats were divided into 2 equal groups, with or without infestation with Trichosomoides crassicauda. The groups were adjusted by feeding "clean" animals the bladders from infested rats, or allowing urine from infested rats to drop on "clean" rats. Infested animals were cleared of worms by adding 0.2% nitrofurantoin to the diet for 8 weeks. Among the experimental animals given 2-acetylaminofluorene in the diet (0.05%; males consumed about 1.3 g and females .97 g/yr.) and sacrificed at 68-70 weeks, there were 5/75 bladder tumors, all in the infested group. There was no significant difference between males and females, and no bladder neoplasms developed in those rats given additional tryptophan (1%) in their diet. The incidence of other tumors was not affected.

70-1172 INHIBITION OF DNA SYNTHESIS AND CHROMOSOME ABERRATIONS IN CULTURED EHRlich ASCITES TUMOR CELLS FOLLOWING TREATMENT WITH LUTEOSKYRIN. (E.) Schachtschabel, D. O. (Philipps U. Inst. Physiol. Chem., Marburg, Germany), F. Zilliken, M. Saito and G. E. Foley. Exp. Cell Res. 57(1):19-28, 1969.

Ehrlich ascites carcinoma cells, treated with the bis-polyhydroxydihydroanthraquinone, luteoskyrin (LS; 1.0 µg/ml), showed a 70% increase in cell number after the first 24 hours, a 25% increase over the next 28 hours until multiplication stopped, a rapid cell loss by day 5, and no cells by day 12. Untreated cultures doubled in about 24 hours. DNA synthesis was reduced 93%, but RNA and protein synthesis maintained about 50-60% activity at 73 hours. The frequency of large multinucleated cells increased (from 1-2% to 6-7%), as did cells which accumulated Sudan Black-positive material. Some cells were resistant to 0.2 µg/ml LS and were eventually adapted to grow in conc. up to 5-10 µg/ml. Certain large chromosomes were noted in 30-40% of cells after 3-5 mo. of cultivation in the presence of LS.

70-1173 SPECIFICITY OF CERTAIN BIOCHEMICAL DERANGEMENTS IN HEPATOCARCINOGENESIS. (E.)

Reid, E. (Chester Beatty Inst. Cancer Res., London). Brit. J. Cancer 24(1):128-137, 1970.

Male rats (200 g) were fed a diet containing either 0.075% α-naphthylisothiocyanate (AN; 0.075%) or DL-ethionine (E; 0.25%) intermittently for over 7 mo. Examination of livers from rats fed AN showed no distinct decrease in nucleotide

levels (even an increase in some cases) and a decrease in microsomal and mitochondrial protein. Livers from E-fed rats showed a decrease in the levels of tri- and diphosphates, with normal levels of monophosphates and no depression of mitochondrial or microsomal protein. A marked rise of the enzymes of uridine monophosphate synthesis was noted in livers and hepatomas from E-fed animals. Both AN and E caused a decrease in mitochondrial acid-soluble nucleotides after 3 weeks and raised the yield of RNA in the supernatant fraction.

70-1174 MECHANISM OF CARCINOGENESIS WITH 1-ARYL-3,3-DIALKYLTRIAZENES - II. IN VITRO-ALKYLATION OF GUANOSINE, RNA AND DNA WITH 1-ARYL-MONOALKYLTRIAZENES TO FORM 7-ALKYLGUANINE. (E.) Preussmann, R. (Max Planck Inst. Immunobiol., Freiburg i. Br., Germany) and A. v. Hodenberg.

Guanosine, yeast RNA and salmon sperm DNA reacted with 1-phenyl-3-monomethyltriazene and 1-phenyl-3-monoethyltriazene to form 7-methylguanine and 7-ethylguanine, resp., as shown by elution chromatography, absorption spectroscopy and thin-layer chromatography. These results indicate that 1-phenyl-3-monomethyl- and monoethyltriazenes act as alkylating agents.

70-1175 PROLONGED ADJUVANT STIMULATION IN GERM-FREE BALB/c MICE: DEVELOPMENT OF PLASMA CELL NEOPLASIA. (E.) McIntire, K. R. (NCI, Bethesda, Md.) and G. L. Princler. *Immunology* 17(3):481-487, 1969.

Term-free (GF), ex-GF (under GF conditions only up to 1-2 mo. of age) and conventional female ALB/c AnN mice were inj. i.p. with 0.5 ml mineral oil at 1-2 mo. of age and again at 2 and 4 mo. The GF animals with neoplasms showed plasma cell tumors (2/33), 16 pleomorphic reticulum cell sarcomas and 7 monomorphic reticulum cell sarcomas. The incidence for the ex-GF mice was 24/31, 3/31 and 1/31, resp., and for the conventional animals it was 28/40, 4/40 and 1/40, resp. Also, antigens (dinitrophenyl-valbumin, Keyhole Limpet hemocyanin, and horse ferritin) were admin. to some GF mice (0.75, 1.5 and 0.75 mg i.p. every 4 weeks) starting at the time of the third mineral oil inoc. None of these mice developed plasma cell tumors. The plasma cell tumors were diagnosed at 11.3 and 15.5 mo. in the ex-GF and conventional mice, resp., but not until 18 mo. in the GF mice.

70-1176 NICKEL CARBONYL INHIBITION OF RNA SYNTHESIS BY A CHROMATIN-RNA POLYMERASE COMPLEX FROM HEPATIC NUCLEI. (E.) Beach, D. J. (Alfred Reed Army Med. Ctr., Washington, D. C.) and F. W. Sunderman, Jr. *Cancer Res.* 30(1):1-50, 1970.

A synthesis by the chromatin-RNA polymerase complex from lysed hepatic nuclei was inhibited

by 52%, 6 hours after inj. of nickel carbonyl ($\text{Ni}(\text{CO})_4$; in LD50 dosage equivalent to 2.2 mg $\text{Ni}/100$ g body wt. i.v.), in 18 male (180-200 g) Sprague-Dawley rats. After an i.v. inj. of $^{63}\text{Ni}(\text{CO})_4$, the liver homogenate contained 0.69% of the radioactivity, and the chromatin-RNA polymerase complex contained 6.6% of the radioactivity in the liver. The av. molar ratio of Ni to DNA nucleotides was 0.046 and the av. conc. of nickel in the final assay mixture was 3.4×10^{-6} M. Addition of $\text{Ni}(\text{CO})_4$ or nickel chloride in vitro did not significantly affect RNA synthesis by the chromatin-RNA polymerase complex from control rats.

70-1177 ARGINASE ACTIVITY IN NICKEL SULFIDE-INDUCED RAT TUMORS. (E.) Hebert, G. J., P. K. Basrur (U. Guelph, Ontario, Canada) and J. P. W. Gilman. *Cancer* 25(5):1134-1141, 1970.

The arginase activity of tumors induced in 12 Fischer rats inj. with nickel sulfide (10 mg, i.m.) was analyzed by incubating tumor homogenate with arginine and measuring urea produced. The enzyme activity was lowest in 1 sclerosing hemangioma (0.009 μmoles urea/mg wet wt.) and was also relatively low in the other tumor of non-skeletal muscle origin (reticulum cell sarcoma; 0.014). The remainder of the tumors were rhabdomyosarcomas, with arginase activity ranging from 0.013-0.122. No enzyme activity was detectable in normal or embryonic muscle, low levels (0.006) in normal muscle from tumor-bearing rats and muscle exposed to nickel sulfide for 24 hours, and high levels in rat liver, especially when incubated with manganese.

70-1178 CHANGES IN MITOCHONDRIAL ULTRASTRUCTURE IN NICKEL SULFIDE-INDUCED RHABDOMYOSARCOMA. (E.) Basrur, P. K. (U. Guelph, Ontario, Canada), A. K. Sykes and J. P. W. Gilman. *Cancer* 25(5):1142-1152, 1970.

Nickel sulfide (10 mg) inj. i.m. into the thigh of Fischer rats induced rhabdomyosarcomas in 11/20 within 3-4 mo. Electron microscopic examination of the tumor cells showed a wide variation in the size of the mitochondria, the larger ones with a large build-up of tubular units, coalescing in groups or forming stacks continuous with the inner mitochondrial membrane or cristae; many showed internal degeneration with replacement by 50-60 Å filaments. These changes were more apparent in the dedifferentiated tumor cells, but aberrant mitochondria were also seen in mitotic cells and myoblasts. Changes were noted as early as 48 hours after exposure to nickel sulfide.

70-1179 POLYRIBOSOME DISAGGREGATION IN RAT LIVER FOLLOWING ADMINISTRATION OF TANNIC ACID. (E.) Reddy, J. K. (U. Kansas Med. Ctr., Kansas City), M. Chiga, C. C. Harris and

D. J. Svoboda. Cancer Res. 30(1):58-65, 1970.

Male F-344 strain rats (125-150 g) were inj. with tannic acid (700 mg/kg s.c.) and sacrificed after fasting overnight. Sedimentation patterns of liver homogenates showed a marked decrease in the polyribosome peak and a significant increase in the monomer and dimer peaks 3 hours after tannic acid admin. Coincident with these changes were the inhibition of ^{14}C -leucine incorporation into liver protein and the observation with the electron microscope of degranulation and vesiculation of the rough endoplasmic reticulum with recovery at about 48 hours.

70-1180 PHAGOCYTIC ACTIVITY OF LEUKOCYTES IN EARLY STAGES OF EXPERIMENTAL CARCINOGENESIS. (Rus.) Korosteleva, T. A. (N. N. Petrov Res. Inst. Oncol., Leningrad, USSR), L. L. Khundanova and Z. M. Chistiakova. Vop. Onkol. 14(11):64-69, 1968.

Non-inbred male rats were fed a diet of 3'-methyl-4-dimethylaminoazobenzene, 4-dimethylaminoazobenzene and acetylaminofluorene (about 10 mg/day of each). Noncarcinogenic analogs of these compounds were fed to controls. In general, both the carcinogenic and noncarcinogenic analogs had the same effects (stimulation or depression) on WBC phagocytic activity in the peripheral blood; these effects were not constant.

70-1181 ELECTRONIC PROPERTIES OF N-HETERO-AROMATICS. XXXI. INTERACTION OF THE CARCINOGEN 4-NITROQUINOLINE 1-OXIDE WITH NICOTINAMIDE. (Jap.) Okano, T. (Tohoku U. Sch. Med. Pharm. Inst., Sendai, Japan) and K. Tsuji. Yakugaku Zasshi (J. Pharm. Soc. Jap.) 89(3):297-301, 1969.

Results of a spectrophotometric study of the interaction of 4-nitroquinoline 1-oxide (4-NQO) with nicotinamide, suggest the formation of a charge-transfer complex, in which the n -electron of the ring nitrogen of nicotinamide is transferred to the π -system of 4-NQO. Solvent effects demonstrated that the new absorption bands arose from this transition.

70-1182 INDUCTION OF BOBBED (bb) MUTATION BY POLYCYCLIC AROMATIC CARCINOGENS IN Drosophila. (E.) Fahmy, O. G. (Chester Beatty Res. Inst. Cancer, London) and M. J. Fahmy. Mutat. Res. 9(2):239-243, 1970.

Male Drosophila melanogaster (+/Y-bb) were inj. in the hemocoel with 7,12-dimethylbenzanthracene (DMBA; 1 mM), 7-bromomethyl-12-methylbenzanthracene (BrM-MBA; 1 mM) or N-benzoyloxy-N-methyl-4-aminoazobenzene (BzO-MAB; 10 mM), mated to marker females (f malbz bb/M-5) at 3-day intervals, and the mutation frequencies in the progeny

fractions (broods) assayed separately. The number of bb mutants always significantly increased in the presence of carcinogens as compared to controls; DMBA induced a 10-fold increase, the others a 3-5-fold increase. The peak mutability of DMBA and BzO-MAB occurred in the first brood, indicating a strong effect on mature sperm, while BrM-MBA exerted its strongest effect on the third brood.

70-1183 THE MUTAGENICITY AND INITIATING ACTIVITY OF SOME AROMATIC AMINE METABOLITES. (E.) Mukai, F. (New York U. Med. Ctr., N. Y.) and W. Troll. Ann. NY Acad. Sci. 163(2):828-836, 1969.

Several carcinogenic derivatives of aromatic amines, such as N-hydroxy-2-aminonaphthalene, N-hydroxy-1-aminonaphthalene, N-hydroxy-2-aminofluorene (N-OH-2AF) and N-acetoxy-2-acetylaminofluorene, were mutagenic when tested on nutritional mutants derived from Escherichia coli; the parent amines were not. When the backs of Swiss-Millerton mice were painted with these derivatives (1 mg), followed in 18 days by croton resin (25 μg ; 3 admin./week), all but N-OH-2AF had tumor-initiating activity. Two other agents, N-hydroxy-2-acetylaminofluorene and 1-hydroxy-2-aminonaphthalene, were carcinogenic but not mutagenic, and did not initiate tumors; N-acetoxy-1-acetylaminonaphthalene and N-acetoxy-2-acetylaminonaphthalene had tumor-initiating activity but were not mutagenic.

70-1184 REACTION OF POLYCYCLIC HYDROCARBON-CYSTEINE CONJUGATES WITH THE AMINOACYL-RNA SYNTHETASE SYSTEM. (E.) Bucovaz, E. T. (U. Tennessee Med. Units, Memphis), J. C. Morrison, H. L. James, C. F. Dais and J. L. Wood. Cancer Res. 30(1):155-161, 1970.

Hydrocarbon-cysteine conjugates, S-(p-chlorophenyl)-L-cysteine (PCP), S-(9,10-dihydro-9-hydroxy-10-phenanthryl)-L-cysteine (DHP), S-(5,6-dihydro-6-hydroxy-5-benz(a)anthryl)-L-cysteine (DHB), S-(5,6-dihydro-6-hydroxy-5-dibenz(a,h)anthryl)-L-cysteine (DHD), and S-(7-benz(a)anthryl)-methyl-L-cysteine (BM) were activated and transferred to transfer RNA using aminoacyl-RNA synthetase derived from bakers' yeast. None of the conjugates were activated by cysteinyl-RNA synthetase, but they did compete with other amino acids; for synthetase enzymes. PCP competed with arginine, DHP competed with glutamic acid, phenylalanine and histidine, DHB and DHD competed with arginine and phenylalanine and BM competed with methionine and leucine.

70-1185 TOXICITY, TISSUE CHANGES, AND TUMOR INDUCTION IN INBRED SWISS MICE BY METHYLNITROSAMINE AND -AMIDE COMPOUNDS. (E.) Frei, J. V. (U. Western Ontario, London, Canada). Cancer Res. 30(1):11-17, 1970.

newborn and 6-8-week-old inbred Swiss mice were given a single i.p. inj. (close to the LD₅₀ value) of dimethylnitrosamine (DMN), methylnitrosourea (MNUA), methylnitrosourethan (MNUN), and methyl nitroso-p-tolylsulfonamide (MNTS). The toxicity of MNUA, MNUN and MNTS was directly proportional to the stability of the compounds. All the compounds induced an increased incidence of pulmonary adenomas (229 tumors in 218 mice). The incidence of lymphomas after treatment with MNUA increased 63-72% in adult and newborn mice of either sex (60/89 with tumors). A sublethal dose of MNUA produced a cell depletion in the lymphoid and especially the myeloid systems, followed by recovery. DMN inj. induced 26 hepatocellular hepatomas in 14/30 newborn mice, but none in adults.

0-1186 THE INITIATION OF SKIN TUMOUR FORMATION IN MICE BY N-HYDROXYCARBAMATES. (E.) Pound, A. W. (U. Queensland Med. Sch., Brisbane, Australia). *Pathology* 1(1):27-33, 1969.

ethyl-N-hydroxycarbamate (40 mg), n-butyl-N-hydroxycarbamate (30 mg), ethyl-N-methyl-N-hydroxycarbamate (40 mg), and n-propyl-N-hydroxycarbamate (25 mg), inj. s.c. into male Hall strain mice (40 mice in each group), followed by topical application of croton oil (1 application/week x 30 weeks, with periodic interruptions), did not significantly increase the number of animals with tumors or the number of tumors/mouse compared to controls (4 tumors in 1/35 animals). However, increased dosage of ethyl carbamate (urethan; 10-40 mg), and ethyl-N-droxy-carbamate (EHC; 20-40 mg) increased both the number of animals with tumors (16/24) and the total number of tumors (48 tumors/25 mice). Treatment with acetic acid prior to inj. with EHC enhanced tumor growth in the few mice studied.

-1187 STRUCTURE-ACTIVITY RELATIONSHIPS AMONG SOME POLYNUCLEAR HYDROCARBONS AND THEIR HYDROGENATED DERIVATIVES. (E.) Lijinsky, A., H. Garcia and U. Saffiotti (NCI, Bethesda, Md.). *J. Nat. Cancer Inst.* 44(3):641-649, 1970.

When admin. by skin painting to female 8-10-week-old Swiss mice, dibenz(a,c)anthracene was weakly carcinogenic, but its 10,11,12,13-tetrahydro derivative was inactive. Dibenz(a,j)anthracene and 1,2,3,4-tetrahydrodibenz(a,j)anthracene were weakly carcinogenic, and 5,6-dihydrodibenz(a,j)anthracene was much more potent than its unsaturated parent; 1,2,3,4,8,9-hexahydrodibenz(a,j)anthracene was inactive. Two dibenz(a)anthracene derivatives, 8,9,10,11-tetrahydro-7,12-dimethylbenz(a)anthracene and 11,12-dihydro-3-methylcholanthrene were both carcinogenic by skin painting. The s.c. inj. of single doses (0.4 mg dissolved in 0.2 ml olive oil) of dibenz(a,h)anthracene and dibenz(a,j)anthracene and their corresponding dihydro, tetrahydro and tetrahydro derivatives revealed significant carcinogenic activity only by dibenz(a,h)-

anthracene and 1,2,3,4-tetrahydrodibenz(a,h)-anthracene, in contrast to skin painting results.

70-1188 CORRELATION OF INITIAL CHANGES IN THE MOUSE EPIDERMAL CELL POPULATION WITH TWO STAGE CARCINOGENESIS - A QUANTITATIVE STUDY. (E.) Major, I. R. (Tobacco Res. Council Labs., Harrogate, England). *Brit. J. Cancer* 24(1):149-163, 1970.

Normal skin from 3-mo.-old male mice was exposed for 5 days to various irritant substances and promoting agents, including cocarcinogen A1, croton oil, tricycloquinazoline, urethan (ethyl carbamate), 1,2-benzanthracene, 3-methylcholanthrene, 1,2,5,6-dibenzanthracene, 1,2,3,4-dibenzanthracene, 1,2,7,8-dibenzanthracene, 7,12-dimethylbenzanthracene, acridine and allyl isothiocyanate and examined for cell number and size, epidermal thickness and mitotic index. Promoting agents were associated with massive and persistent hyperplasia, whereas irritant substances induced more frequent cellular degeneration.

70-1189 A COMPARISON OF THE ONCOGENICITIES OF 3-HYDROXYXANTHINE, GUANINE 3-N-OXIDE, AND SOME RELATED COMPOUNDS. (E.) Sugiura, K. (Sloan-Kettering Inst. Cancer Res., New York, N. Y.), M. N. Teller, J. C. Parham and G. B. Brown. *Cancer Res.* 30(1):184-188, 1970.

Female Wistar and Sprague-Dawley rats (80-100 g) were inj. with 3-hydroxyxanthine (0.1-7.0 mg) or guanine 3-N-oxide (0.1-3.0 mg; 1 admin./week x 22 or 26 weeks, s.c. in the scapular region). The weekly dose required for 50% tumor induction was between 0.1-0.5 mg, with no significant difference in potency or latent period. The low tumor induction by other purine derivatives, 1-hydroxyxanthine and 6-mercaptopurine 3-N-oxide, indicated that both the position of the N-oxide and other substituents influenced the oncogenicity. Adenine 1-N-oxide had moderate oncogenicity, while xanthine, guanine, adenine, 6-hydroxylaminopurine, 6-mercaptopurine and 2-aminopurine had almost none.

70-1190 A NEW INBRED STRAIN OF MOUSE C17/lcr DEVELOPED FOR TESTING WEAK CARCINOGENS. (E.) Ranadive, K. J. (Tata Mem. Ctr. Cancer Res. Inst., Bombay, India), S. V. Gothoskar and G. Fernandes. *Indian J. Med. Res.* 57(3):521-527, 1969.

A female albino XVII strain mouse was mated with a male C57BL/lcr mouse, and the progeny with a light brown coat (C17/lcr) selected and inbred for 25 generations. These mice were good breeders, with a long life-span and few spontaneous lesions (an over-all incidence of less than 1% over 12 yr.). Swiss/lcr and C17/lcr were compared as to their sensitivity to various skin

carcinogens. Admin. of 3-methylcholanthrene (0.3%; 2 admin./week x 13 weeks) induced 100% tumors in both strains. Admin. of an acetone extract of tobacco, partially and completely free of alkaloids E₉ and E₁₀ (2%; 2 admin./week) and croton oil (3%; 1 admin./week from week 12 to death), induced papillomas and carcinomas in 35.7% and 0% in the Swiss mice and 51.7% and 20% in the C17 mice, resp. Similar application of Chinar tar and croton oil for a max. of 60 weeks in Swiss mice induced 61.3% gross papillomas and 6.4% frank carcinomas, compared to 57.9% and 21.1%, resp., after 42 weeks of treatment in the C17 strain. Other very weak carcinogens (such as peanut oil or mustard oil) induced skin tumors in C17/lcr mice.

70-1191 PATHOLOGY OF EXPERIMENTAL NEUROGENIC TUMORS CHEMICALLY INDUCED DURING PRENATAL AND POSTNATAL LIFE. (E.) Wechsler, W. (Max Planck Inst. Brain Res., Cologne, Germany), P. Kleihues, S. Matsumoto, K. J. Zülch, S. Ivankovic, R. Preussmann and H. Druckrey. Ann. NY Acad. Sci. 159(2):360-408, 1969.

Experimental induction of neurogenic tumors by topical and systemic application of carcinogens is described in relation to understanding the pathogenesis of such tumors naturally occurring in man. A large experimental series on the neurocarcinogenic effect of N-nitroso compounds admin. by various routes to postnatal, or transplacentally to fetal BD rats is discussed. Incidence of tumor type, dose effect and time relationship, autoradiographic experiments measuring DNA synthesis and cell generation cycle, and some ultrastructural detail of tumor cells are presented.

70-1192 PROTEIN SYNTHESIS IN HUMAN LEUKOCYTES AND LYMPHOCYTES: I. EFFECT OF STEROIDS AND STEROLS. (E.) Werthamer, S. (Methodist Hosp., Brooklyn, N. Y.), C. Hicks and L. Amaral. Blood 34(3):348-356, 1969.

The *in vitro* effects of the sterols, cholesterol and 3-methylcholanthrene (3-MC), and the steroids, hydrocortisone (H; cortisol), prednisolone (P) and testosterone (T), on protein synthesis in separate populations of human WBC and lymphocytes were studied. All of these agents inhibited protein synthesis. Whereas the inhibitory mechanism of H, P and T required the presence of plasma, 3-MC inhibited amino acid incorporation in its absence. The inhibitory response of lymphocytes to 3-MC (17%) was greater than that produced in WBC incubations (8%). When present in conjunction with either H or T, 3-MC increased the percentage of inhibition. The results suggest that 3-MC inhibits amino acid incorporation by a different mechanism, and at a different site of the lymphocyte, than the other agents.

70-1193 CHEMICAL STRUCTURE AND CARCINOGENICITY OF ALIPHATIC HYDRAZO, AZO, AND AZOXY COMPOUNDS AND OF TRIAZENES, POTENTIAL *IN VIVO* ALKYLATING AGENTS. (E.) Preussmann, R. (Preventive Med. Res. Group, Freiburg, Germany), H. Druckrey, S. Ivankovic and A. v. Hodenberg. Ann. NY Acad. Sci. 163(2):697-714, 1969.

Aliphatic hydrazo, azo and azoxy compounds, and aryl dialkyltriazenes are discussed in relation to carcinogenicity, structure-activity relationships and possible mode of action. Azoxymethane and 1,2-dimethylhydrazine, admin. s.c. or p.o., induced a high incidence of carcinoma of the colon and the rectum in BD rats. Malignant neoplasms of the brain, olfactory bulb, mammary gland or liver, as well as leukemias, but not intestinal tumors, were induced by 1,2-diethylhydrazine, azo- and azoxyethane. The carcinogenicity of certain triazenes was shown by the induction of malignant tumors of the brain, nervous system and kidneys in the BD rat. These agents were probably converted *in vivo* to carcinogenic alkylating agents.

70-1194 PHYSIOLOGICAL GENETICS OF MELANOTIC TUMORS IN *Drosophila melanogaster*. VI. THE TUMORIGENIC EFFECTS OF JUVENILE HORMONE-LIKE SUBSTANCES. (E.) Bryant, P. J. (U. California, Irvine) and J. H. Sang. Genetics 62(2):321-336, 1969.

Larvae of *Drosophila melanogaster* strain *tu bw;+su-tu*, carrying a melanotic tumor gene with a penetrance of about 90%, were placed in continuous contact with compounds having juvenile growth hormone activity. Farnesyl methyl ether (FME), dodecyl methyl ether and farnesoate derivative (with the most potent hormone activity and carcinogenicity), increased the av. number of tumors/fly, while less active hormones reduced tumor frequency; this suppression might be related to a non-hormonal effect. FMA and farnesoate derivative induced tumors during the second or first larval instar; no abnormalities of the ring gland or timing of the molting process were seen in the tumor strains. No tumors were induced by FME in strains not carrying the melanotic tumor gene.

70-1195 URINARY EXCRETION OF CARCINOGENIC TRYPTOPHANE METABOLITES IN CANCER OF BLADDER. (E.) Bapna, B. C. (All-India Inst. Med. Sci, New Delhi), S. M. Singh and A. Nath. Indian J. Med. Res. 57(3):586-588, 1969.

Urine (25 ml + 1 ml glacial acetic acid) from 22 pts. with bladder cancer and from 15 normal healthy subjects was placed in a freezer, passed through a deactivated charcoal column, and the dried residue compared to a standard soln. of 3-hydroxyanthranilic acid (3-HOA) by ascending paper chromatography. In 14/22 cancer pts., a

greater quantity of 3-HOA was excreted than in the normal subjects and in 5/8 pts. treated surgically; less 3-HOA was excreted postoperatively than before the operation.

70-1196 NONENZYMATIC FORMATION OF CINNABARINIC ACID IN URINE OF PATIENTS WITH TUMORS OF THE URINARY BLADDER. (E.) Nishimura, R. (Tulane U. Sch. Med., New Orleans, La.), G. E. Pipkin, G. A. Duke and J. U. Schlegel. Invest. Urol. 7(3):206-214, 1969.

An identical UV spectrum and chromatogram was seen for cinnabaric acid (compound IV) and the oxidative products formed in urine (25 ml) from bladder tumor pts. and normal subjects after overnight incubation with 3-hydroxy-anthranilic acid (3-HOA) at 37° C. Compound IV was found in the urine of 9/18 from the nontumor group (excluding heavy smokers), compared to 11/15 (73%) samples from bladder tumor pts., which also showed greater amounts of compound IV. No compound IV was found in the urine of either group after incubation with 3-HOA, when the urine samples contained high ascorbic acid levels following ascorbic acid admin. (500 mg, 3 doses/day p.o.).

70-1197 EFFECT OF ANTITHYMOCYTE SERA ON THE GROWTH OF PLASMA CELL TUMORS IN MICE. (E.) Mandel, M. A. (Univ. Hosps. Cleveland, Ohio) and J. J. DeCosse. Surg. Forum 20:109-111, 1969.

Antithymocyte sera (ATS - 0.5 ml) was inj. into 3 groups of 50 BALB/c mice, followed by s.c. inj. of 5×10^4 MPC 37 plasma cell tumor cells. Tumors were detected in normal mice inoc. with 5×10^4 tumor cells in 3-4 weeks and all were dead by 9 weeks. In mice receiving ATS on the day of tumor inoc., tumors were apparent at 2 weeks and all were dead at 4.5 weeks. Tumor growth was accelerated when the ATS was inj. 3, but not 7, days prior to tumor cell implantation. The effect of ATS was reversed by inj. of 75×10^6 immunologically competent syngeneic spleen cells 2 days after (but not the day of or 7 days after) tumor and ATS inj. The ratio of tumor size and serum level of immunoglobulin $\gamma 2b$ was unchanged by ATS. Similar results were observed using MOPC 104E plasma cell tumor cells.

70-1198 CARCINOGEN-INDUCED TUMORS OF THE THYMUS. IV. HUMORAL INFLUENCES OF NORMAL THYMUS AND FUNCTIONAL THYMOMAS AND INFLUENCE OF POSTTHYMECTOMY PERIOD ON RESTORATION. (E.) Stutman, O. (U. Minnesota Med. Sch., Minneapolis), E. J. Yunis and R. A. Good. J. Exp. Med. 130(4):809-819, 1969.

Neonatally thymectomized strain A or C3Hf/Bi mice, inj. 5-50 days later with syngeneic or allogeneic thymus or cells of a 7,12-dimethyl-benzanthracene-induced thymoma (s.c. or i.p.,

or contained within an i.p. diffusion chamber), showed a progressive decrease in effectiveness of immunological restoration with delay of treatment (from 80% to 13%). Only multiple thymus grafts (syngeneic or allogeneic) were effective (up to 65%) in restoring neonatally thymectomized A or C3Hf/Bi mice after the onset of the wasting syndrome (usually after 50-75 days). Single grafts of thymus, thymomas, or diffusion chambers containing thymus or thymoma, were ineffective. Wasted mice could also be restored with i.p. inj. of spleen cells from neonatally thymectomized, 5-day-old syngeneic mice plus s.c. implantation of thymomas. Spleen cells from a 45-day-old mouse were ineffective.

70-1199 THE INDUCTION OF MURINE NEOPLASIA. (E.) Keast, D. (U. Western Australia, Perth) and N. F. Stanley. Pathology 1(1):19-26, 1969.

A graft-versus-host reaction was produced in 120 newborn Prince Henry (PH) mice by i.p. inj. of 10^6 - 10^7 spleen cells from Royal Perth Hospital (RPH) mice of various ages. Of 65 mice that survived longer than 35 days, further passage of spleen cells from one mouse led to the development of a lymphoma (designated 553/L) centered at the mesenteric lymph nodes. No malignant neoplasms developed in 30 newborn PH mice after inj. with RPH spleen cells and gaging with neomycin sulfate to deplete intestinal organisms. Treatment of newborn PH mice with spleen cells from adult PH mice induced a thymic lymphoma in 1/247 animals.

70-1200 THE MURINE RUNTING SYNDROME AND NEOPLASIA. (E.) Keast, D. (U. Western Australia, Perth). Immunology 16(6):693-697, 1969.

Prince Henry mice were runted by 0.5-0.1 ml bacterial endotoxin from their own intestinal flora (inj. i.p. every 48 hours up to 260 days of age; about 20-50 μ g/inoc. up to weaning and then 100 μ g/inoc.). Of the mice kept acutely toxic for the first 10 days, several which died between 70-120 days had only remnants of thymus; some developed an arthritic condition of the hindlimbs, but no neoplasms; 10-15% developed overgrown teeth. From 70 days of age, several spindle cell sarcomas, thymic lymphomas and 1 cystic development of the frontal air sacs in the skull developed. Tumor incidences after this and other runting procedures were compared. Acute treatment with endotoxin raised the tumor incidence to 8.3% (4/48); chronic treatment to 2.0% (1/50); and neonatal reovirus-3 infection to 1.75% (not significantly different from the control value of 0.42%). No tumors developed in mice admin. bacterial vaccine or cortisone therapy, or in mice with a chronic graft-versus-host reaction. Spleen cells from 1 mouse with runting induced by chronic graft-versus-host reaction, and from 1 mouse with reovirus-3-induced runting, induced a lymphoma in neonatal mice.

70-1201 GRISEOFULVIN AND CHRONIC GRANULOCYTIC LEUKAEMIA. (E.) König, E. (Ruhr U. Med. Clin., Essen, Germany), K. Berthold, H. A. Hienz and G. Brittinger. Helv. Med. Acta 35(2): 103-107, 1969.

A 48-yr.-old woman was treated for dermatomycosis (tinea) with griseofulvin (500 mg/day, total 3 g over 3 mo.). At that time the spleen was not palpable and the blood picture was normal. After 6 mo., a routine blood study revealed a WBC of 30,800 with a shift to the left in the granulocytic cells. The bone marrow was hypercellular with increased immature granulopoietic cells and a mild eosinophilia. Typical signs of chronic granulocytic leukemia developed over the next few mo. (splenomegaly, no detectable alkaline phosphatase in the peripheral granulocytes and the presence of the Ph¹ chromosome in bone marrow cells). The karyotype demonstrated an extra submetacentric chromosome similar to those of group B, and the absence of a group C chromosome.

70-1202 COMBINED CARCINOGENESIS WITH POLYOMA VIRUS AND 2-ACETYLAMINOFLUORENE. (E.) Smith, R. D. (U. Illinois Coll. Med., Chicago). Fed. Proc. 28(2):298, 1969.

70-1203 FLUORESCENT ANTIBODY STUDIES OF CHEMICAL AND VIRUS-INDUCED THYMIC LYMPHOMAS IN C57BL MICE. (E.) Doell, R. G. (Stanford U., Calif.). Fed. Proc. 28(2):314, 1969.

70-1204 DIFFERENTIAL INHIBITORY EFFECT ON MOUSE LIVER DNA SYNTHESIS BY 9,12-DIMETHYLBENZANTHRACENE IN RELATION TO THE MITOTIC CYCLE AFTER PARTIAL HEPATECTOMY. (E.) Raick, A. N. (U. Toronto Banting Inst., Canada) and A. C. Ritchie. Fed. Proc. 28(2):365, 1969.

70-1205 EFFECT OF 3-METHYLCHOLANTHRENE ON URIDINE DIPHOSPHATE GLUCURONYLTRANSFERASE. (E.) Howland, R. D. (U. California San Francisco Med. Ctr.) and A. Burkhalter. Fed. Proc. 28(2): 417, 1969.

70-1206 BIOTRANSFORMATION OF 3-METHYLCHOLANTHRENE; STIMULATION OF ITS OWN METABOLISM. (E.) Bresnick, E. (Baylor U. Coll. Med., Houston, Tex.) and H. Mosse. Fed. Proc. 28(2): 417, 1969.

70-1207 BIPHASIC DECREASE IN RADIOACTIVE HEMOPROTEIN OF THE CO-BINDING PARTICLES: EFFECT OF 3-METHYLCHOLANTHRENE (3-MC). (E.) Levin, W. (Burroughs Wellcome & Co. Res. Labs., Tuckahoe, N. Y.) and R. Kuntzman. Fed. Proc. 28(2):483, 1969.

70-1208 EARLY EFFECTS OF PHENOBARBITAL (PB) AND 3-METHYLCHOLANTHRENE (MC) ON RNA TRANSCRIPTION IN RAT LIVER. (E.) Wold, J. W. (U. Iowa, Iowa City) and W. J. Steele. Fed. Proc. 28(2):484, 1969.

70-1209 THE ROLE OF IMMUNITY TO TUMOR-SPECIFIC TRANSPLANTATION ANTIGENS IN THE DEVELOPMENT OF PRIMARY TUMORS INDUCED IN MICE WITH 3-METHYLCHOLANTHRENE. (E.) Haughton, G. (U. North Carolina Sch. Med., Chapel Hill), J. Wagner and E. Sigmon. Fed. Proc. 28(2):568, 1969.

70-1210 POSSIBLE MECHANISMS FOR ADRENAL NECROSIS AFTER 7,12-DIMETHYLBENZANTHRACENE. (E.) Harris, C. (Philadelphia Geriat. Ctr., Pa.). Fed. Proc. 28(2):579, 1969.

70-1211 ABNORMAL PROLIFERATIVE EFFECTS OF THE GAS PHASE OF CHARCOAL FILTERED FRESH CIGARETTE SMOKE ON 3T3 CELLS. (E.) Leuchtenberger, C. (Swiss Inst. Exp. Cancer Res., Lausanne), R. Leuchtenberger, J. Blanchard and M. Deckert. Fed. Proc. 28(2):683, 1969.

70-1212 ENDOCRINE ALTERATION OF MAMMARY PARENCHYMAL CELL UPTAKE OF CARCINOGEN. (E.) Janss, D. H. (U. Tennessee Med. Units, Memphis) and R. C. Moon. Fed. Proc. 28(2):684, 1969.

70-1213 IN VITRO AND IN VIVO STUDIES OF INTESTINAL ABSORPTION OF AROMATIC POLYCYCLIC HYDROCARBON CARCINOGENS. (E.) Rees, E. D. (U. Kentucky Coll. Med., Lexington), P. Mandelstam and J. Lowry. Fed. Proc. 28(2):749, 1969.

70-1214 CHEMOPROPHYLLAXIS OF BENZO(RST)PENTAPHENE CARCINOGENESIS BY ORANGE OILS, d-LIMONENE AND d-LIMONENE AND d-LIMONENE HYDROPEROXIDE. (E.) Homburger, F. (Bio-Res. Inst., Cambridge, Mass.), A. Treger and E. Boger. Fed. Proc. 28(2):749, 1969.

See also abstract nos.: 993,995,996,997,998,999,1000,1001,1002,1004,1005,1007,1011,1014,1017,1018,1020, 1021,1022,1023,1024,1036,1039,1041,1253,1297,1337,1340,1368

- 70-1215 A NEW VIRUS OF MINIMAL PATHOGENICITY ASSOCIATED WITH FRIEND VIRUS. I. ISOLATION BY END-POINT DILUTION. (E.) Rowson, K. E. K. (U. London Inst. Laryng. Otol.) and I. B. Parr. Int. J. Cancer 5(1):96-102, 1970.

During an attempt to purify a strain of Friend virus (FV) by passage in BALB/c mice at end-point dilution, a new virus was obtained and referred to as the Rowson-Parr virus (RPV). The new virus was passaged by plasma 7 times at 21-day intervals and regularly produced minor splenomegaly which did not progress. RPV was present in the plasma of infected animals for at least 122 days and the spleen did not return to normal, but the infection was not lethal. Mice infected with RPV developed gross splenomegaly after a subsequent inj. of FV, but the disease progressed more slowly than in mice infected with FV alone. Neutralizing FV antibodies were not demonstrated in plasma of RPV-infected mice. On filtration through gradocol membranes, RPV appeared to be the same size as FV; it was chloroform-sensitive, resistant to terramycin and did not affect the plasma lactate dehydrogenase level of infected mice.

- 70-1216 A NEW VIRUS OF MINIMAL PATHOGENICITY ASSOCIATED WITH FRIEND VIRUS. II. HISTOLOGICAL CHANGES AND IMMUNODEPRESSIVE EFFECT. (E.) Carter, R. L. (Chester Beatty Res. Inst., London), F. C. Chesterman, K. E. K. Rowson, M. J. Salaman and N. Wedderburn. Int. J. Cancer 5(1):103-110, 1970.

Histological reactions induced in BALB/c mice by the Rowson-Parr virus were primarily confined to the spleen and consisted of moderate splenomegaly (200-350 mg) associated with red pulp hyperplasia, especially in the perifollicular zones, and enlargement and activation of the germinal centers. There was no proliferation of plasma cells at any time. A severe depression of the immune response to sheep RBC was seen between days 2-6 after infection; a more moderate immunodepression was detected up to 6 mo. or more after infection.

- 70-1217 EFFECT OF BONE MARROW GRAFT ON THE SUSCEPTIBILITY OF MICE TO FRIEND LEUKEMIA VIRUS. (E.) Odaka, T. (Inst. Med. Sci., Kanawa, Tokyo). Jap. J. Exp. Med. 39(1):99-100, 1969.

Bone marrow cells from Friend Leukemia virus (FLV)-resistant C57BL/6 (B6) mice and from FLV-susceptible C57BL/6-Fv^s (B6-S) mice were inj. v. into B6-S mice which had been heavily irradiated with ⁶⁰Co. After 3 hours or 1 day, each mouse was inj. i.p. with 10^{4.1} mouse infective dose₅₀ of FLV and sacrificed in 10-21 days. All mice which had received B6 marrow cells showed no splenomegaly, while the mice receiving B6-S marrow had marked splenomegaly and a higher

virus titer. This suggests that the susceptibility locus (Fv) was expressed on bone marrow cells and is transferable.

- 70-1218 EFFECTS ON LEUKEMOGENESIS OF THE PURIFICATION AND CONCENTRATION OF AN ACCELLULAR EXTRACT OF A CHLOROMA DERIVED FROM FRIEND'S LEUKEMIA. (Fr.) Chamorro, A. (Radium Inst. Pasteur Lab., Paris). C. R. Soc. Biol. (Paris) 163(10):2015-2017, 1969.

As contrasted to animals inoc. with the raw, acellular extract of a solid chloroma induced by Friend leukemia (0.1 ml, single i.p. dose), neonate mice inoc. with the same dose of a purified conc. (50%) of extract showed a reduction of the mortality rate from 45% to 8%, an increase of successful leukemogenesis from 55% to 62%, an increase of the proportional number of Friend leukemias from 64% to 87%, and a corresponding reduction of the proportional number of myeloid leukemias from 35% to 12%. The reduction of mortality rate is attributed to elimination (during the process of purification) of germs pathogenic to the neonate mice.

- 70-1219 THE SUPPRESSIVE EFFECTS OF RAUSCHER LEUKEMIA VIRUS ON THE SECONDARY ANTIBODY RESPONSE OF SPLEEN CELLS CULTURED IN CELL-IMPERMEABLE DIFFUSION CHAMBERS. (E.) Borella, L. (U. Tennessee Med. Units, Memphis). J. Immun. 103(2):185-195, 1969.

BALB/c mice, inoc. with Rauscher leukemia virus (RLV; 0.2 ml i.p.) and receiving sheep RBC (SRBC) at various times thereafter, showed a time-related depression of antibodies (Ab) from 0 hours to 3 days for 7S Ab and 19S Ab, resp. BALB/c mice, given SRBC 7 days after inoc. with RLV, demonstrated a larger erythroblastic response and a greater depression of anti-SRBC Ab than the partially-RLV-sensitive C57BL strain, suggesting that both effects are secondary to RLV infection. Resistance to both the immunosuppression and erythroblastosis was seen in mice inoc. i.p. with 0.25 ml anti-RLV. When spleen cells, primed with SRBC, were cultured with SRBC in cell-impermeable diffusion chambers and implanted in irradiated isogenic mice, Ab production and plasmacytosis were observed. There was a suppression of Ab formation when diffusion chambers containing primed spleen cells and SRBC were placed in mice inoc. i.p. with SRBC, when chambers containing primed spleen cells and irradiated RLV-infected spleen cells were placed in a normal mouse, and when chambers containing normal spleen cells and SRBC were placed in RLV-infected hosts.

- 70-1220 CHARACTERISTICS OF A TUMOR CELL LINE AND VIRUS DERIVED FROM HAMSTER TUMORS INDUCED BY RAUSCHER LEUKEMIA VIRUS-TRANSFORMED

HAMSTER EMBRYO CELLS. (E.) Rhim, J. S. (NCI, Bethesda, Md.), R. J. Huebner, R. C. Ting, N. Wivel and W. Vass. Int. J. Cancer. 5(1):28-32, 1970.

A transplantable hamster tumor (RHT-1), induced by Rauscher leukemia virus-transformed hamster embryo cells, was established in secondary Swiss NIH mouse tissue culture (NIH-METC). The tumor cell line contained group-specific complement-fixing antigen and continuously released infectious virus. This cell line contained Type C particles. The virus derived from this cell line served as helper virus for a defective Moloney sarcoma virus (MSV) from a non-infectious hamster tumor (HT-1), and rescued infectious MSV by direct superinfection of the HT-1 cells. The infectious MSV virus (MSV(RLV)) readily produced foci in both hamster embryo cells and NIH-METC. Foci produced by this MSV(RLV) pseudotype in hamster embryo cells consisted mostly of spindle-shaped cells that stained brightly with acridine orange. Tumors were produced when cell-free supernatants of MSV(RLV)-transformed hamster embryo cells, or the cells themselves, were inj. into newborn mice, and also when transformed cells were inj. into newborn hamsters.

70-1221 NEOPLASTIC TRANSFORMATION OF RAT EMBRYO CELLS INDUCED IN VITRO BY RAUSCHER LEUKEMIA VIRUS. (E.) Rhim, J. S. (NCI, Bethesda, Md.), R. J. Huebner, W. T. Lane and M. L. Vernon. Proc. Soc. Exp. Biol. Med. 133(3):914-920, 1970.

Rauscher leukemia virus (RLV) induced neoplastic transformation in primary cultures of NIH-METC and Fisher rat embryo cells. These cells, initially infected with RLV, replicated the infectious virus and produced complement-fixing (CF) antigen that was characteristic of the leukemia-sarcoma virus complex for 18 mo. and longer. Cells derived from these cultures underwent neoplastic transformation in vitro and induced tumors when inj. into homologous hosts. These tumors were serially transplantable and further transplants carried the initial RLV and produced CF antigen.

70-1222 RAT EMBRYO CELLS IN COMPLEMENT FIXATION TESTS FOR MURINE LEUKAEMIA VIRUS. (E.) Rhim, J. S. (NIH, Bethesda, Md.) and R. J. Huebner. Nature (London) 226(5246):646-647, 1970.

Cultures of secondary NIH-mouse embryo (ME), rat embryo (RE) and passage 11 RE cells were infected with 10^4 infectious units of Rauscher leukemia virus (RLV): a complement fixation titer of 1:32 was obtained in ME and RE cells, while 1:8 was produced in the continuous RE cell line. In a second experiment, endpoint titers of RLV were found to be the same in ME and RE cells. All RE cells derived from different rat strains yielded complement fixation antigens comparable to ME cells, the highest titer being that for

the strain OM rats. Further testing for comparative sensitivity in ability to produce complement fixation antigen of various established murine leukemia and sarcoma virus strains produced titers in RE cells as high as, or higher than, those obtained in ME cells in almost all instances. These results indicate that RE cells are useful for propagation and assay of murine leukemia and sarcoma viruses cultured in vitro. RE cells may have advantages for the isolation of certain viruses.

70-1223 STUDIES ON THE PATHOGENESIS AND MECHANISM OF HEMATOLOGIC DIVERSIFICATION BY RE-ISOLATION OF THE MYELOID LEUKEMIA VIRUS (GRAFFI). (E.) Fey, F. (German Acad. Sci. Inst. Cancer Res., Berlin-Buch). Acta Haemat. (Basel) 42(2):65-75, 1969.

Newborn strain XVII Bln. mice were inoc. s.c. with virus from cell-free filtrates of various leukemias and, after 5-20 days, filtrates from their organs were admin. to similar mice. With myeloid leukemia virus, there was a max. leukemogenic action using liver and spleen filtrates prepared on day 10 with moderate diversification as to leukemic type produced. Paramyeloblastic leukemia virus produced distinct leukemogenic activity seen only with spleen filtrates and after a long latent period. There was considerable diversification. Thymic filtrates of lymphatic leukemia demonstrated strong leukemogenic activity by day 10 with much diversification; spleen and bone marrow filtrates had weak activity. For the reticular leukemia, only the thymic filtrates had a strong leukemogenic activity by day 10 and diversification was minimal.

70-1224 SIGNIFICANCE OF THE SPLEEN IN THE PATHOGENESIS OF VIRUS INDUCED LEUKEMIAS OF MICE. (Ger.) Fey, F. (German Acad. Sci. Inst. Cancer Res., Berlin-Buch). Z. Ges. Inn. Med. 24(16):511-513, 1969.

Graffi leukemia virus (GLV), obtained from myeloid, paramyeloblastic lymphatic and reticulum cell leukemias, was inoc. into newborn Strain XVII mice; 5-20 days later; cell-free extracts from tissues of these mice were inoc. into another group of newborn Strain XVIII mice. GLV isolated from mice with myeloid leukemias showed the highest leukemogenic activity; splenic extracts were more leukemogenic than thymic extracts (leukemias developed in 84% and 40-45% of recipient mice, resp.), while brain extracts showed negligible activity. Leukemias pathologically identical to the original leukemias were most frequent in mice inj. with GLV derived from cell-free spleen extracts of mice with myeloid leukemia (77% of the leukemias induced by these cell-free extracts were chloroleukemias). It is suggested that the spleen is the main site for the pathogenetic processes of myeloid and paramyeloblastic leukemias, the thymus for the reticulum

all and lymphatic forms. The role of Graffi virus-sensitive target cells of the spleen is discussed in relation to the leukemia-inhibiting effect of splenectomy.

-1225 POSSIBLE INHERITED LEUKAEMOGENIC FACTORS IN FAMILIAL ACUTE MYELOGENOUS LEUKAEMIA. (.) Snyder, A. L. (NIH, Bethesda, Md.), E. S. Anderson, E. P. Li and G. J. Todaro. Lancet 7647):586-589, 1970.

kindred in which 6 cases of acute myelogenous leukemia and 2 cases of malignant reticuloendotheliosis developed over 3 generations is described. Laboratory tests for susceptibility of skin fibroblasts to SV40-transformation showed that fibroblast-cell strains from the proband, her mother and her sister had 5-50 times the expected number of transformed colonies, but normal transformation frequencies were found among maternal relatives. Abnormal immunoglobulin levels were detected among maternal relatives; the highest IgM levels were in the proband's mother and in the mother of the children with reticuloendotheliosis. There may be a correlation between familial abnormalities of immunoglobulin levels and increased susceptibility to malignancy. The presence of unusually susceptible individuals and relatively common environmental factors may contribute to the high frequency of leukemia in this family.

7-1226 VIRAL INDUCED ACUTE LYMPHATIC LEUKEMIA IN GUINEA PIGS RESEMBLING HUMAN LEUKAEMIA. (E.) Opler, S. R. (Stanford U. Sch. Med., Calif.). Haematologia 3(2):157-162, 1969.

Leukemia was induced in Strain 2 guinea pigs by injection of cell-free leukemic plasma (1 ml of a 1:1000 dilution, s.c.). The incubation period varied from 12-60 days. The bone marrow was flooded with lymphoblasts, with rare megakaryocytes, granulocytes or normoblasts. Lymphoblasts predominated in the peripheral blood and the number of granulocytes was markedly reduced. Foá-Kuloff cells with inclusion bodies and a flattened nucleus were also seen. Electron microscopy of leukemic cells demonstrated viral particles budding into the cisternae of the endoplasmic reticulum. Immature virus had a less electron dense intermediate layer than known murine leukemia viruses. Mature Type C particles were seen in the intracellular spaces, but not budding from the cell membrane. All organ systems were infiltrated with the lymphoblasts, and the spleen and mesenteric lymph nodes were greatly enlarged.

7-1227 SURVIVAL OF MOUSE SKIN ISOGRAFTS FROM LEUKEMIC DONORS. (E.) Meeker, W. R., Jr (Roswell Park Mem. Inst., Buffalo, N. Y.), E. J. Mirand and J. T. Grace, Jr. J. Surg. Oncol. 1(1):19-22, 1969.

Newborn inbred DBA/2 mice were injected with cell-free filtrate (0.1 ml, s.c.) from spleens of mice with 334-C virus-induced leukemia. After 4 weeks, a skin graft was made to recipient mice, some of which were immunized with 3 weekly injections of 10^7 - 10^8 viable 334-C leukemic cells from Swiss mice starting at 1 week of age. No significant difference was observed between the survival of the graft in the non-immunized (88.4%) and immunized (87.5%) mice. Similar results were obtained using Swiss Hauschka/ICR mice and 334-C virus. However, when skin from DBA/2 mice with Friend-virus-induced leukemia was grafted, 50% of the immunized mice rejected the graft as opposed to 30% of the non-immunized. In a mouse strain (adult C57B1/Ha) naturally immune to induction of Friend leukemia, all grafts were rejected.

70-1228 MURINE LEUKEMIA. (Sp.) Pasqualini, C. D. (Nat. Acad. Med. Inst. Hemat. Res., Buenos Aires, Argentina), F. Saal and S. L. Rabasa. Medicina (B. Air.) 28(Suppl. 1):116-124, 1968.

Serial, cellular transplants of 31 mouse leukemias and 11 mouse tumors in five different, inbred strains were maintained with many of the passages repeated every 8-15 days, because the transplants prove fatal to the hosts within that period. The leukemias appeared to acquire the morphologic and cytogenetic characteristics of the host strain, whether they arose spontaneously or were induced by i.p. inoculation of ^{32}P or Sarcoma 180, intrasplenic implant of human lymphomatous biopsy material, Burkitt's lymphoma cells cultured *in vitro*, and cells of allogeneic leukemias, irradiation, or treatment with 3-methylcholanthrene. Short-latency leukemias (less than 50 days) were induced in BALB mice by both implant of human lymphoma cells and implant of allogeneic AKR leukemia cells, as above. The AKR leukemia (induced by Gross leukemia virus) cells were characterized by the presence of an antigen associated with that virus, the antigen also appearing in association with the secondary, BALB strain, leukemia. It is concluded that these short-latency leukemias were induced when pre-existing Type A virus particles, characteristic of the BALB strain in the absence of treatment, were activated by some triggering factor present in the xenogeneic or allogeneic malignant cells inoculated into the susceptible host, resulting in the development of Type C particles, which were responsible for the actual leukemogenesis.

70-1229 SPONTANEOUS LEUKEMIA IN FISCHER RATS. (E.) Moloney, W. C. (Child. Cancer Res. Found., Boston, Mass.), A. E. Boschetti and V. P. King. Cancer Res. 30(1):41-43, 1970.

A mononuclear cell leukemia was observed in 21/86 inbred female rats derived from Dunning's Fischer 344 line. The average duration of the

disease was 5 weeks, and the ages at death ranged from 14-30 mo. (median 25 mo.). Peripheral blood smears showed WBC count from 18,000-158,000/mm³ as well as nucleated RBC's and marked polychromasia. The mononuclear cells did not contain alkaline phosphatase, peroxidase or esterase in the cytoplasm; there was no acid phosphatase in the granules; and stains for oil red O and periodic acid Schiff were negative. Chromosomal analysis of 4 animals showed one with one or 2 extra chromosomes in over 50% of the metaphases and one with an extra chromosome in autosomes 4-10 in over 50% of the metaphases.

70-1230 ISOLATION OF A RNA-DEPENDENT RNA POLYMERASE FROM VIRUS INFECTED MYELOBLASTS. (E.) Watson, K. F. (Columbia U. Inst. Cancer Res., New York, N. Y.) and G. S. Beaudreau. Biochem. Biophys. Res. Commun. 37(6):925-932, 1969.

RNA-dependent RNA polymerase was obtained from 100 g of frozen myeloblast cells from chicks in the terminal stages of myeloblastic leukemia and separated into 4 fractions during purification (S-0 to S-3), the S-3 fraction having the highest enzyme activity. Enzyme activity was dependent on the addition of a heteropolymer form of RNA, and in the presence of polyvinyl sulfate, high molecular wt. RNA from myeloblastosis virus was the most effective template. The requirement for homologous RNA was not absolute as RNA from Q β bacteriophage and from Escherichia coli also was able to serve as a template.

70-1231 OCCURRENCE, PATHOLOGICAL FEATURES, AND PROPAGATION OF GONADAL TERATOMAS IN INBRED MICE AND IN RABBITS. (E.) Meier, H. (Jackson Lab., Bar Harbor, Me.), D. D. Myers, R. R. Fox and C. W. Laird. Cancer Res. 30(1):30-34, 1970.

The pathology was described of spontaneous gonadal teratocarcinomas in a 6-mo.-old female CBA/J mouse, a female weanling DBA/2J mouse, a 4-mo.-old male DBA/2J mouse, a male 2-week-old A/HeJ mouse and a testicular teratoma in a 3-mo.-old strain III male rabbit. All but the A/HeJ testicular tumor were propagated in vitro, and except for the rabbit tumor, successfully transplanted in an isologous animal. Complement fixation tests for murine leukemia viruses were strongly positive with both DBA/2J teratomas and yielded virus in SWR/J and C57L/J, but not BALB/c mouse embryo cell cultures. Primary and transplanted tumors and tissue cell cultures of the CBA/J ovarian teratocarcinoma were complement fixation negative.

70-1232 LACK OF EVIDENCE FOR ONCOGENIC OR AMYLOID INDUCING QUALITIES OF Mycoplasma neurolyticum INOCULATED INTO BALB/C MICE. (E.) Ebbesen, P. (U. Copenhagen Inst. Med. Microbiol.)

and K. Lind. Acta Path. Microbiol. Scand. 76(4):594-600, 1969.

Inbred BALB/c mice were inoc. with 10⁴ colony forming units (c.f.u.) of Mycoplasma neurolyticum intranasally (i.n.) in 0.1 ml broth, or 10³-10⁵ c.f.u., i.p., or s.c. in 1.0 ml broth. The highest incidence of leukemia was seen in uninoc. mice, and was not affected by inoc. with M. neurolyticum. Females had a higher incidence (25%) than males (5%) and most of the leukemias developed in old mice. Mostly, the leukemias were type-B reticulosarcomas, with 4 lymphocytic and 1 granulocytic leukemia. Amyloidosis developed only in males, but was unrelated to inoc. with M. neurolyticum.

70-1233 IDENTITY AND NATURE OF ISOLATED LYMPHOID TUMORS (SO-CALLED NODAL HYPERPLASIA, HAMARTOMA, AND ANGIOMATOUS HAMARTOMA) AS REVEALED BY HISTOLOGIC, ELECTRON MICROSCOPIC, AND HETEROTRANSPLANTATION STUDIES. (E.) Fisher, E. R. (VA Hosp., Pittsburgh, Pa.), J. C. Sieracki and D. M. Goldenberg. Cancer 25(6):1286-1300, 1970.

Case histories were reviewed of an 11-yr.-old Caucasian female and a 42-yr.-old Caucasian male with primary nonlymphomatous tumors of the lymph nodes. Cells similar to Reed-Sternberg cells were seen in both tumors, but no other characteristics of a malignant lymphoma were observed. The girls' tumor was composed mainly of lymphocytes with some plasma cells and reticulum cells, the sinusoidal architecture was intact and there was no capsular infiltration with atypical cells. Electron microscopic examination of the tumor from the male revealed reticulum cells similar to those seen in reticulum cell sarcoma, and virus-like particles similar to those seen in murine and human leukemias and lymphomas. These membrane-bound particles were also seen in tumors and metastases induced by this growth in cheek pouches of male golden hamsters.

70-1234 FURTHER STUDIES ON THE MURINE SARCOMA VIRUS (HARVEY) COMPLEX - ISOLATION OF A MURINE LEUKAEMIA VIRUS. (E.) Turano, A. (U. Parma Inst. Microbiol., Italy), F. Tedeschi and G. Fadda. Ig. Mod. 61(11-12):993-1005, 1968.

Swiss outbred (133), Balb/c (90) and C57Bl/6 inbred (69) mice were inj. s.c. with 0.2 ml cell-free filtrate from cells infected with Parma leukemia virus (PLV) and at 3 mo. demonstrated enlarged spleens and lymph nodes typical of lymphoid generalized leukemia. The histology of the spleen, thymus and other organs were described. The cytoplasm of mouse sarcoma virus-infected cells showed a diffuse yellow-green fluorescence after treatment with fluorescent antisera against PLV or the Friend-Moloney-Rauscher leukemia virus complex. B269 cells

derived from a Moloney sarcoma virus-induced aneuploid tumor), cocultivated with Swiss mouse embryo cells with 0.1 ml PLV or Moloney leukemia virus, induced tumors in 12/18 and 8/13 newborn Swiss mice, resp.

1235 INHIBITORY EFFECT OF STATOLON ON MURINE LEUKEMIA AND SARCOMA VIRUSES IN CELL CULTURE. (E.) Rhim, J. S. (NCI, Bethesda, Md.), J. Huebner and S. Gisin. Antimicrob. Agents Chemother. 190-193, 1968.

Mouse embryo tissue cultures were exposed for 24 hr. to various conc. (0-100 µg/ml) of statolon prior to infection with the Moloney strain of mouse sarcoma virus (MSV) or Friend leukemia virus (FLV). There was a dose-related inhibition of focus-forming units of MSV, and in the case of FLV, no leukemia virus or complement fixation antigen was detectable in cultures treated with 100 µg/ml. Inhibition was still observed when statolon was added with the virus or 24 hr. later. There was no inhibition after heating the statolon at 121°C for 15 min. No direct action on viruses was seen.

1236 COMPARATIVE ELECTRON MICROSCOPIC STUDY OF ROUS SARCOMA IN SYRIAN HAMSTER AND RAT. (E.) Lindberg, L. G. (U. Lund Inst. Path., Sweden). Acta Path. Microbiol. Scand. 76(4):349-360, 1969.

Electron microscopy of sarcomas induced in Syrian hamsters and rats by the Schmidt-Ruppin strain of Rous sarcoma virus demonstrated 2 distinct types of cells, seen in both species, which could be grouped according to the ultrastructure of the nucleus. The nucleus of cells classified as A cells was large, rounded or oval, with dense nucleoli and a scanty chromatin as opposed to the nucleus of cells classified as C cells, which is smaller and more elongated with less distinct nucleoli and heavy clumping of chromatin. Polyribosomes, a normal plasma membrane, and a distinct nuclear membrane was seen in both groups. Golgi system was regularly seen in A cells but rarely in C cells, whereas lysosomes were more common in C cells, but were few and small. Other morphological similarities between the tumor cells of the 2 species were compared.

1237 THE OCCURRENCE OF VIRUS PARTICLES IN ROUS HAMSTER SARCOMA. (E.) Lindberg, L. G. (U. Lund Inst. Path., Sweden). Acta Path. Microbiol. Scand. 76(4):520-528, 1969.

Viral particles were seen with the electron microscope in primary and serially transferred in vivo and in vitro Rous hamster (RHa) sarcomas induced by the Schmidt-Ruppin strain of Rous sarcoma virus inoc. i.m. in Syrian hamsters. Production of viral particles was most prominent

in the later passages of the serially transferred in vivo lines and only in severely damaged cells; viral particles in hamster sarcoma cultures appeared somewhat different and were seen in slightly damaged cells. Morphology is described. Typical virus-producing Rous chicken sarcoma cells were induced 14-25 days after inoc. of RHa-sarcoma cells from in vivo tumors i.m. into 10 chickens. However, culture medium from RHa-sarcoma cells or homogenates of in vivo RHa-sarcomas were unable to induce tumors after inoc. into chickens or newborn hamsters, or to transform cells in vitro.

70-1238 GROWTH OF ROUS HAMSTER SARCOMA ON THE CHORIO-ALLANTOIC MEMBRANE. (E.) Ahlström, C. G. (U. Lund Inst. Path., Sweden) and L. G. Lindberg. Acta Path. Microbiol. Scand. 77(1):49-56, 1969.

A suspension of $0.5-2 \times 10^6$ Rous hamster sarcoma cells, induced by the Schmidt-Ruppin strain of Rous sarcoma virus (RSV), was inoc. into the chorio-allantoic membrane (CAM) of 9-day-old embryonated eggs of RIF-free chickens. Hemorrhagic or white plaques appeared after about 7 days, and were composed of hamster sarcoma cells. A second passage to CAM produced similar results, but after a third passage, the CAM developed lesions not unlike those induced by RSV and were found to be composed almost entirely of Rous chicken sarcoma cells. Cell-free extracts of this membrane induced sarcomas after inj. into wing webs of RIF-free chicks. It was seen that during the first few days after inoc. of hamster sarcoma cells on the CAM, a close contact was established with the mesodermal chicken cells, which was thought to possibly facilitate transfer of RSV.

70-1239 EXAMINATION OF VARIOUS AVIAN SPECIES FOR NEUTRALIZING ANTIBODY AND SUSCEPTIBILITY TO ROUS SARCOMA VIRUS. (E.) Rabin, H. (Zool. Soc. San Diego Inst. Compar. Biol., Calif.) and W. J. L. Sladen. Amer J. Epidemiol. 89(3):325-330, 1969.

In 17 species of birds examined, only free-living young domestic chickens had antibody to the Bryan strain of Rous sarcoma virus (RSV). No antibodies to the Schmidt-Ruppin strain were found in 6 types of gallinaceous birds including domestic chickens. No evidence of virus production or cell transplantability was seen in tissue cultures of embryos of Redwinged Blackbirds, Common Grackles, Green Herons, and Black Ducks after incubation with the Bryan strain of RSV; cells from Japanese Quail embryos successfully transplanted. Tumors were produced after inoc. of either virus i.m. in the wing of Red Jungle Fowl and Japanese Quail; Pekin Ducks, Starlings, and Brown-headed Cowbirds were resistant to both viruses, and the Guinea Fowl was resistant to the Bryan strain.

70-1240 BRAIN TUMORS INDUCED IN DOGS BY THE SCHMIDT-RUPPIN STRAIN OF ROUS SARCOMA VIRUS. NEUROPATHOLOGICAL AND IMMUNOLOGICAL OBSERVATIONS. (E.) Bigner, D. D. (Duke U. Med. Ctr., Durham, N. C.), G. L. Odom, M. S. Mahaley, Jr. and E. D. Day. J. Neuropath. Exp. Neurol. 28(4): 648-680, 1969.

Mongrel pups were inoc. on the second day of life with 10^8 PFU of Schmidt-Ruppin Rous sarcoma virus in the mid-portion of the right cerebral hemisphere. The tumor incidence in all dogs inoc. with virus that lived past 1 week was 86% (30/35). The various tumor types were 19/30 having gliomas only, 8/30 having both gliomas and sarcomas, and 3/30 having sarcomas only. Almost all glial tumors observed in humans were observed except oligodendrogliomas and medulloblastomas. All dogs that did not develop tumors had bacterial infections, and 2 dogs had both. Autopsy revealed no metastases of any tumors and a high incidence of hydrocephalus, about half due to obstruction by tumor or infection, and half due to an in-apparent cause. About 50% of the dogs with tumors, infection, or Kaolin-induced hydrocephalus showed generalized or focal neurological symptoms. Cytology of the cerebrospinal fluid was definitely positive for malignancy in 11/17 dogs developing tumor, and possibly positive for the remainder.

70-1241 TUMOR INDUCTION IN ADULT MICE BY SR-RSV MATERIAL WITH SYNGENEIC EMBRYO CELLS. (E.) Takeuchi, M. (U. Tokyo Inst. Med. Sci., Takanawa) and T. Yamamoto. Jap. J. Exp. Med. 39(3):233-238, 1969.

Chicken tumor cells (CTC), containing Schmidt-Ruppin Rous sarcoma virus (SR-RSV), were mixed with cells from 12-14-day-old C3H/He, DDD or C57BL/6 mouse embryos and inj. s.c. into syngeneic mice. Tumors developed at the site of inoc. in all mice, even after passaging the mixture *in vitro* 15 times before inj. These tumors could only develop and be passaged in syngeneic mice. No tumors were induced using chicken tumor cells (CTC) alone, or mouse embryo cells (MEC) alone. When MEC were incubated with culture fluid from CTC, which contained RSV, the latent period was 2-3 weeks longer. Culture fluid from the cell mixture or from the CTC alone could not induce tumors, nor could cell-free lysates of MEC inj. together with virus or CTC. When C3H/He MEC were passed 2-3 times before mixing, tumor growth was slowed and incidence decreased.

70-1242 STUDIES ON ROUS SARCOMA VIRUS IN MICE. III. THREE LINES OF SR-RSV-INDUCED MOUSE ASCITES SARCOMA. (E.) Takeuchi, M. (U. Tokyo Inst. Med. Sci., Takanawa) S. Hino and T. Yamamoto. Jap. J. Exp. Med. 39(3):239-251, 1969.

Solid tumors of C3H/He and DDD mice, induced by chicken tumor cells containing Schmidt-Ruppin Rous sarcoma virus, were converted to an ascites tumor after i.p. inoc. into syngeneic mice. An

ascites sarcoma was produced in C57BL/6 mice after i.p. inoc. of cells from the 2008 sarcoma strain induced by SR-RSV-infected chorioallantoic membrane. Induction of tumors in the wing-webs of Rock-horn chickens by the DDD ascites sarcoma was stable with respect to latent period (11-17 days), survival (about 31 days), and tumor incidence (60-100%). The older generations of the C57BL/6 ascites tumor showed a decreased incidence of wing-web tumors (generations 14-40 induced 33-47%; generations 60-80 only 25.8%). Cloning of the DDD and C57BL/6 ascites tumors in syngeneic newborn thymectomized mice, and chromosomal analysis of the tumor cells are described.

70-1243 RETARDATION OF PROTEIN SYNTHESIS IN RAT TUMOURS ON INHIBITING HISTAMINE FORMATION. (E.) Grahn, B. (U. Lund Inst. Physiol., Sweden) and E. R. E. Rosengren. Experientia 26(2):125-126, 1970.

Histamine forming capacity (HFC) was determined in Walker 256 mammary carcinosarcoma and Rous virus sarcoma tissue, with or without the histidine decarboxylase inhibitors, α -methyl histidine (MH) or 4-bromo-3-hydroxy benzyloxyamine (NSD-1055). HFC was higher in Rous sarcoma than in Walker 256 tumor; in Rous tumor, 2.5 mM DL- α -methyl histidine depressed histamine formation by about 80%, and in Walker 256 tumor inhibition was inconsistent and in 2 cases had no effect. The NSD-1055 (0.5 mM), used in Rous sarcoma only, strongly depressed histamine formation. The rate of leucine incorporation was about the same in the soluble and insoluble protein fractions in both tumors. In Walker 256 tumor, leucine incorporation under the influence of MH (2.5 mM) was approx. 80% of control values in both protein fractions. This indicated that this tumor to a minor extent, or not at all, depends on nascent histamine for its growth. In Rous tumor, either of the inhibitors depressed leucine incorporation into both protein fractions by about 50%.

1244 CELL-MEDIATED AND HUMORAL IMMUNE REACTIONS AGAINST TUMOUR-SPECIFIC AND VIRAL ANTIGENS IN RELATION TO ROUS SARCOMA VIRUS TUMORIGENESIS IN RATS. (E.) Jonsson, N. (U. Lund Inst. Path., Sweden). Acta Path. Microbiol. Scand. 77(4):753-755, 1969.

Lymph-node-cell (LNC) suspensions and sera from inbred-strain R/F rats bearing tumors induced by s.c. inoc. of Schmidt-Ruppin Rous sarcoma virus (RSV) 3-6 days after birth, exhibited colony inhibition on allogeneic rat tumor cells in 16/20 and 12/20 cases, resp. No relationship to the latency period or tumor growth time was demonstrated. Colony inhibition by LNC was observed with 10/15 rats in which tumors failed to grow, and with sera from only 4. Neutralizing antibodies for RSV were found in 1 rat in each group.

0-1245 THE CONTINUED NEED FOR DNA SYNTHESIS FOR REPLICATION OF ROUS VIRUS IN CELLS PREVIOUSLY INFECTED WITH A RELATED VIRUS. (Fr.) Jigier, P. (Radium Inst., Orsay, France). C. R. Acad. Sci. [D] (Paris) 270(8):1192-1195, 1970.

our hr. to 7 days after infection of a secondary culture of chick embryo fibroblasts by avian lymphoma virus (RAV-1), the cultures were rein- fected with Schmidt-Ruppin strain Rous sarcoma virus, then incubated for 1-3 days in the presence of 5-bromodeoxyuridine or cytosine arabinoside. Inhibition of the replication of the Rous sarcoma virus by both agents was the same in the pre- treated cultures as it was in control cultures in- fected with Rous sarcoma virus alone. It is concluded that the mechanism (involved in viral replication) which depends upon early DNA syn- thesis is not synthesis of an enzyme which can be used for replication by all of the viruses of the same group, or production of a viral constituent of cellular origin which is common to all.

0-1246 DEMONSTRATION OF A BICATENOID RNA IN A CELL LINE TRANSFORMED AND CHRONICALLY INFECTED WITH MOUSE SARCOMA VIRUS. (Fr.) Van Riensven, L. (St. Louis Hosp. Inst. Leukemia Res., Paris), R. Emanoil-Ravicovitch and M. Boiron. C. Acad. Sci. [D] (Paris) 270(13):1723-1726, 1970.

Cell line 78 A₁, isolated in the authors' labora- tory from Wistar rat embryo fibroblasts trans- formed by Moloney mouse sarcoma - mouse leukemia virus *in vitro* and producing the virus continu- ously, was cultured in a medium containing 10% casein hydrolysate and labeled by 48 hr. incuba- tion with tritiated uridine (2 µc/ml), prior to differential centrifugation, and separating the nuclear and cytoplasmic elements, as verified by electron microscopy. The cells contained "heavy" RNA, with a molecular wt. of 1×10^7 daltons, visible into sub-units weighing $2-3 \times 10^6$ daltons. Treatment of the separated nuclear and cytoplasmic elements with DNase and RNase demonstrated the presence in the nuclear element, alone, of a nucleic acid fraction which was resistant to both RNases and which was not demonstrable in rat embryo fibroblasts not infected with the virus. This fraction was resistant to RNase at high ionic strength, but completely hydrolyzed at low ionic strength, with no comparable difference demonstrable with respect to DNase, confirming that it was a bicatenoid RNA. A fusion temperature of 97° C indicated a guanosine + cytosine content of 44%. It is concluded that this bicatenoid RNA was the replicating form of the virus.

7-1247 MURINE SARCOMA VIRUS: THE QUESTION OF DEFECTIVENESS. (E.) Parkman, R. (Bethesda, Md.), J. A. Levy and R. C. Ting. Science 168(3929):387-389, 1970.

and mouse cells infected by the murine sarcoma virus (MSV) [Moloney isolate] showed 2-hit kinetics of focus production in mouse cells, but 1-hit

kinetics in rat cells. Addition of antiserum to cultures after infection gave suppressed focus formation in mouse, but not rat, cells. In rat cells infected with MSV, leukemia virus is not essential for focus formation and these foci re- sult from proliferation of the transformed rat cell. In mouse cells, the leukemia virus is required as helper and focus formation requires spread of virus. If the term defectiveness is used, it should not be applied to RNA tumor viruses without qualification for the viral function studied and the cell system used.

70-1248 CYTOTOXIC POTENTIAL OF DIFFERENT LYMPHOID CELL POPULATIONS AGAINST CHROMIUM-51 LABELLED TUMOUR CELLS. (E.) Pearson, G. R., R. J. Hodes and S. Friberg, Jr. (Karolinska Inst., Stockholm). Clin. Exp. Immun. 5(3):273-284, 1969.

C57BL and ASW mice were immunized with 1 ml (inj. in equal portions i.p. and to each extremity) of $1-3 \times 10^6$ viable tumor cells (virus-induced sarcoma in CBA mice (Ha3); spontaneous mammary carcinoma in ACA mice; and methylcholanthrene-in- duced tumors in CBA mice) or 10×10^6 spleen cells. Lymphoid cells from immunized mice had more cytotoxicity against ^{51}Cr -labeled target cells (as measured by release of ^{51}Cr) used as antigens, than lymphoid cells from non-immunized mice or from mice immunized against non-cross- reacting antigens. Cells immunized against strong or weak antigenic determinants on Ha3 cells both showed strong specific cytotoxicity. Peritoneal exudate cells were slightly more effective than spleen cells and both were much more effective than lymph node cells. Exogenous complement was not required.

70-1249 ST-FELINE FIBROSARCOMA VIRUS: INDUC- TION OF TUMORS IN MARMOSSET MONKEYS. (E.) Deinhardt, F. (Presbyterian-St. Luke's Hosp., Chicago, Ill.), L. G. Wolfe, G. H. Theilen and S. P. Snyder. Science 167(3919):881, 1970.

Newborn and 3-day-old marmoset monkeys were inoc. s.c. and i.p. with tumor homogenate or cell-free tumor extract from an experimentally-induced feline fibrosarcoma. No signs of tumor develop- ment were seen in the animals given tumor homogen- ate, but after 4 weeks, palpable masses were observed in the right inguinal areas of both animals given extract. At necropsy, lesions were absent at the site of s.c. inoc., but both had inguinal and multiple intra-abdominal fibro- sarcomas. The tumor cells were either fusiform or polygonal with 46 chromosomes and a normal karyotype; no viral particles were seen under the electron microscope.

70-1250 ON PLASMOCYTOMA - ONCOGENESIS OF MICE. EVOLUTION OF A POORLY DIFFERENTIATED SARCOMA (HIPA TUMOR OF BALB/c MICE) INTO A

PLASMOCYTOMA. IV. A COMPARATIVE HISTOLOGICAL AND ELECTRON MICROSCOPIC STUDY. (E.) Pedio, G. (U. Zurich Histopath. Inst., Switzerland), E. Grieshaber and J. R. Rüttner. Path. Microbiol. (Basel) 34(2):65-85, 1969.

An HIPA mesenteric sarcoma with hemorrhagic ascites was induced in BALB/c mice by i.p. inj. of isologous spleen homogenate from a mouse pretreated with incomplete Freund's adjuvant; this sarcoma gradually transformed into a plasmocytoma. Histologically, after the first 2 transplantations, the mesenteric tumor nodules consisted of poorly differentiated cells, most of which were spindle-shaped, interspersed with a large number of collagen fibers. Electron microscopy showed a well-developed Golgi complex and an ergastoplasm of low density. From the third to the twenty-sixth generation, the spindle-shaped cells decreased as undifferentiated polygonal cells increased, with immature plasma cells at various stages of differentiation appearing here and there. Electron microscopic examination showed the polygonal cells undergoing a gradual differentiation characterized by the appearance of annulate lamellae and an increase in rough endoplasmic reticulum. Numerous virus-like particles, similar to type 'C', were also seen. From the twenty-seventh generation on, fully developed plasma cells were predominant, with some at various stages of differentiation. The electron microscope showed a well-developed Golgi complex with a highly-organized endoplasmic reticulum, but no viral particles.

70-1251 ON PLASMOCYTOMA - ONCOGENESIS OF MICE. V. VIRUSES AND VIRUS RELATED STRUCTURES IN HIPA TUMOR. (E.) Grieshaber, E. (U. Zurich Histopath. Inst., Switzerland), G. Pedio and J. R. Rüttner. Path. Microbiol. (Basel) 34(2):86-97, 1969.

Virus-like particles were first observed in the fifth generation in the evolution of a poorly-differentiated sarcoma of BALB/c mice (HIPA tumor) into a plasmocytoma, becoming numerous between the sixth and twenty-sixth transplantations. The viruses, similar to type 'C', were mainly in the extracellular space, with other particles in the vesicles, vacuoles or inclusion bodies of immature cells. Aggregates of particles with various shapes, but the same basic structure, were found in the cytoplasm of undifferentiated cells near the cell surface (sixth and eighth generations). Intracellular clusters of unusual granules were found in spindle-shaped cells and also have been seen in young plasma cells. A decrease in the virus-like particles was observed in the thirty-second and thirty-seventh generations, and no viruses were seen in tumors consisting of well-differentiated plasma cells (more than the forty-second generation).

70-1252 THE DISTRIBUTION OF THE MOUSE MAMMARY TUMOR AGENT AND ITS ANTIGENICITY IN

MILK. (E.) Miroff, G. (Union Coll., Schenectady, N. Y.) and H. V. Lamberson. Int. J. Cancer 5(1):136-146, 1970.

The mammary tumor agent and a specific soluble antigen in the milk of inbred mice that develop mammary tumor were found in approx. equal proportions in both supernatant and pellet after ultracentrifugation. Over 90% of the agent and the highest antigen titer were found in a density range of 1.06-1.075 in ficoll density gradients. Low tumorigenic potential and antigenicity of the B particle band remained with the particles after removal of proteinaceous contaminant by gel filtration. Tumorigenic material isolated from ECTOLA and carboxymethylcellulose chromatographic columns did not show a high positive correlation with the distribution of the virus-like B particles. The antigen found with the B particles and the lower molecular wt. active component were immunologically identical.

70-1253 INHIBITION OF SPONTANEOUS BREAST TUMOURS IN A HIGH MTV STRAIN. (E.) Mody, J. K. (Tata Mem. Ctr. Cancer Res. Inst., Bombay, India), M. H. Gavankar and K. J. Ranadive. Indian J. Cancer 6(2):61-65, 1969.

An inbred female C3H(Jax) mouse, totally mam-mectomized before puberty, was mated with a homologous inbred male, and the litter (F1 generation) was foster nursed on a Swiss strain breeder and inbred, starting a new strain C3H/Mect at the twenty-first generation. Spontaneous adenocarcinomas of the breast were seen in 7/75 (9.3%) breeders and in none of 46 virgins. These mice are extremely sensitive to induction of cancer by 7,12-dimethylbenzanthracene admin. locally or systemically.

70-1254 RELEASE OF LEUKEMIA C PARTICLES FROM MURINE CELL LINES INFECTED WITH BITTNER VIRUS-CONTAINING INOCULA. (E.) Lasfargues, E. Y. (Inst. Med. Res., Camden, N. J.), N. Pillsbury, J. C. Lasfargues and D. H. Moore. Cancer Res. 30(1):167-178, 1970.

Embryo and mammary tissue cultures of C57BL/Haag mice were inoc. with milk from RIII mice, B particles from RIII milk or extracts of a tumor induced in a C57BL mouse by RIII milk. Inoc. caused continuous growth of all cell lines with no distinct morphological differences from controls in the early mo., but changes were noted after 3-4 mo. Electron microscopic studies showed abundant type C virus particles in all inoc. cell lines, especially cell cultures inoc. with tumor extract, and rarely in control cultures. Serological analysis indicated that the cell lines are positive for complement fixation with polyvalent leukemia antiserum and for immunofluorescence with leukemia antiserum, but negative with mammary tumor virus antiserum inj. (i.p. or s.c.) into BALB/c and C57BL mice induced sarcomas at the site of inj. for all 3 cell lines.

70-1255 STUDIES ON THE HERPES-TYPE VIRUS RECOVERED FROM THE BURKITT'S TUMOR AND OTHER HUMAN LYMPHOMAS. (E.) Stewart, S. E. (NIH, Bethesda, Md.). Advances Virus Res. 15:291-305, 1969.

The organs and the susceptible population affected by Burkitt's tumor (BL) is discussed along with its geographical distribution and environmental factors. The herpes-like virus isolated from BL tissue culture is compared to that in other normal and neoplastic cell cultures. It was noted that a reovirus was also found. Finally, the biological action of the virus was reviewed and immunologic evidence of its role in BL and infectious mononucleosis presented. (84 references)

70-1256 PREVALENCE, INCIDENCE AND PERSISTENCE OF EB VIRUS ANTIBODY IN YOUNG ADULTS. (E.) Niederman, J. C. (Yale U. Sch. Med., New Haven, Conn.), A. S. Evans, L. Subrahmanyam and R. W. McCollum. New Eng. J. Med. 282(7):361-365, 1970.

Indirect immunofluorescent tests on the sera of 1084 young adults showed a prevalence of Epstein-Barr virus (EBV) antibody ranging from 26% in incoming Yale freshmen (ages 17-18) to 87% among Colombia military recruits (ages 18-20). Among 150 Yale students, tested upon admission between 1958-1963 and again in 1968, 53 initially had EBV antibody, only 2 of whom had a previous clinical history of infectious mononucleosis (IM), and all remained positive; 65 had no evidence of EBV antibody and no clinical history of IM in the first series, but over the next 4-8 yr., 43 acquired EBV antibody, only 28 with evidence of IM. The incidence of infection was 11.1%/yr., and the increment in prevalence from 35% at age 17-18 to 64% 4-8 yr. later. EBV antibody was present in the serum of Yale students as long as 8 yr. after clinical or sub-clinical infection.

0-1257 DNA SYNTHESIS IN EB VIRUS-CONTAINING BURKITT LYMPHOMA CULTURES DURING A TEMPERATURE CYCLING PROCEDURE. (E.) Maurer, B. (Roswell Park Mem. Inst., Buffalo, N. Y.), L. Glick and J. Minowada. Proc. Soc. Exp. Biol. Med. 133(3):1026-1030, 1970.

The pattern of DNA synthesis in 2 Burkitt lymphoma (BL) cell lines was studied during temperature cycling and temperature reduction (32°) experiments; P3JHR1K (HR1K), an Epstein-Barr virus (EBV)-containing clone and P-1 Raji (P1R), an EBV-free cell line, were used. Direct and indirect immunofluorescent tests for EBV-related antigen were employed. Temperature cycling or temperature reduction procedures applied to EBV-containing BL cells usually produced cultures that had a higher incidence of EBV-containing cells than non-treated cultures. EBV-free BL cells exhibited a loss in viability and reduction rate of DNA synthesis when subjected to these

procedures. When HR1K and P1R cultures were subjected to a temperature cycling or reduction procedure, both exhibited a reduced rate of DNA synthesis compared to noncycled counterparts. DNA was synthesized in cycled HR1K cultures at a faster rate than cycled P1R cultures, but in noncycled HR1K cultures, DNA synthesis, relative to that in noncycled P1R cultures, was synthesized at similar rates. The data indicate that in HR1K cultures, cells exist in 2 forms, a virion-free form that synthesizes DNA at a slower rate than the second form, a virus-producing cell. The DNA synthesized by EBV-containing cells is probably EBV DNA.

70-1258 IMMUNOFLUORESCENT STUDIES USING FRACTIONATED IMMUNOGLOBULIN OF SERA OF FOWLS WITH MAREK'S DISEASE. (E.) Naito, M. (Osaka U. Res. Inst. Microbial Dis., Japan), K. Ono, S. Tanabe and S. Kato. Biken J. 12(4):257-261, 1969.

Strains of herpes-type virus were isolated in duck embryo fibroblasts (DEF) from the blood of 3 De Karb 161 chickens showing signs of Marek's disease (MD). The globulins were separated from the sera obtained from these birds, labeled with fluorescein isothiocyanate, and the conjugated dye separated into 2 fractions by DEAE-cellulose chromatography. Fraction 2 (eluted with 0.5 M sodium chloride) from each of the 3 sera or from the pooled sera, showed complete cross-reactivity, producing fluorescence in both the cytoplasm and nuclei of all infected cells. Burkitt lymphoma cells, the P3 strain of P3HR-1, and chick kidney cells infected with avian adenovirus were stained with sera from one of the chickens with MD and with the pooled sera, but no fluorescence was seen.

70-1259 DIFFERENCE BETWEEN ONCOGENIC AND NON-ONCOGENIC HUMAN ADENOVIRUSES IN PLAQUE FORMING ABILITY IN AN ESTABLISHED CALF KIDNEY CELL LINE. (E.) Kimura, S. (Tokushima U. Sch. Med., Japan), K. Fukui and N. Yoshida. Biken J. 12(2):129-131, 1969.

Human adenovirus types 1, 2, 3, 5, 6, 7, 8, 9, 12, 13, 14, and 18 were inoc. on monolayers of calf kidney cells (CKC), and after 12 days of incubation, plaques were counted. Types 1, 2, 5, 6, 8, 9, and 13 (no oncogenicity in hamsters) produced clear plaques and types 3, 7, 12, 14, and 18 (oncogenic in hamsters) produced no plaques even with larger inocula. Furthermore, types 1 and 5 were able to grow in CKC, while types 3, 7, and 12 could not.

70-1260 EFFECT OF ONCOGENIC DNA VIRUSES ON REGULATORY MECHANISMS OF CELLS. (E.) Green, M. (St. Louis U. Sch. Med., Mo.). Fed. Proc. 29(3):1265-1275, 1970.

Expression of viral genes in virus-free cells transformed by groups A, B and C human adenoviruses (Ad) showed that 3 classes of virus-specific RNA molecules differing in base sequence are transcribed in transformed cells: one specific for group A adenoviruses (Ad 12, 18 and 31), one for group B (Ad 3, 7, 11, 14, 16 and 31) and a third specific for group C (Ad 1, 2, 5 and 6). The ratio of cellular to viral DNA ranged from 5×10^3 to 2×10^4 in 7 different Ad 2, 7 and 12 transformed cell lines, corresponding to from 20-80 viral gene copies per cell. In studies on the fraction of the viral genome transcribed in Ad 2 transformed cells and early and late during productive infection with Ad 2, it was found that the Ad 2 genome possessed from 23-46 genes, 8-20% of the viral genome is transcribed early after infection, at 6 hours, before viral DNA synthesis, and 4-10% of the viral genome is transcribed in Ad 2 transformed rat embryo cells. Only a small fraction of the viral genome functions in the transformed cell. The results of these and other studies show that a large number of viral DNA copies is integrated in the transformed cell, certain viral gene sequences are selectively transcribed and the functions of only several viral genes are required for maintaining the transformed state of the cell.

70-1261 VIRUS NEUTRALIZING ANTIBODIES AGAINST ADENOVIRUS TYPE 18 IN PATIENTS WITH NEOPLASTIC DISEASES AS COMPARED TO THE NORMAL POPULATION. (Ger.) Tauchnitz, C. (Johannisallee 32, Leipzig, Germany), E. Luschnitz and H.-P. Keller. Z. Ges. Inn. Med. 24(8):114-115, 1969.

Sera determinations from 170 cancer pts. and 424 controls revealed adenovirus 18 neutralizing antibodies in 27.1% of all cancer pts. and 41.5% of healthy subjects. Sera (1:10 dilution) from pts. with bronchial (37), mammary (40), and genital organ carcinomas (22) and various sarcomas (25) frequently contained significantly less antibodies (24.3%, 22.5%, 9.1% and 20.0%, resp.) than sera from a mixed carcinoma group (45.7%) or from controls (41.5%). Results were similar for the 1:5 dilution. No differences in frequency of hemagglutination-inhibiting antibodies against parainfluenza virus type 1 were seen, and there was no correlation with severity and course of the disease.

70-1262 DEVELOPMENT OF TUMORS IN HAMSTERS BY IN UTERO INJECTION OF ADENOVIRUS TYPE 12 INTO FETUSES. (E.) Fukui, K. (Tokushima U. Sch. Med., Japan), S. Kimura, Y. Sagara, T. Aoki and N. Yoshida. Biken J. 12(2):125-126, 1969.

Pregnant hamsters were anesthetized with ether, the uterus exposed, and 0.02 or 0.04 ml of adenovirus 12 strain Huie (10^3 - 10^4 TCID₅₀) was inj. into the fetuses by various routes 2-9 days prior to delivery. No tumors developed in 8/15 controls born alive; in 15/23 inj. with 10 and 400 TCID₅₀; or in 32 fetuses inoc. in the amniotic cavity

with 20 TCID₅₀. Of 31 fetuses inj. intracranially and 20 inj. i.p. with 200 TCID₅₀, all were aborted but 8, which died within 5 days. Tumors were seen s.c. in 1/13 newborn animals inj. intrapleurally with 200 TCID₅₀ and in 2/5 inj. with 400 TCID₅₀. No tumors were seen in 41 hamsters whose mothers received virus i.v., nor could virus be isolated from fetuses obtained 30-180 min. after i.v. inj. of pregnant hamsters.

70-1263 BASE COMPOSITION OF DNA IN ADENOVIRUS-12-INDUCED TUMOR. (E.) Ohmori, M. (Okayama U. Med. Sch., Japan). Acta Med. Okayama 23(6):593-597, 1969.

Tissue from Huie-strain adenovirus 12-induced tumors from 2-week-old Syrian hamsters was found, by Ogur-Rosen's method, to contain 3.6 mg RNA/g fresh tumor tissue (ftt) and 14.2 mg DNA/g ftt; by Schneider's method, 3.8 mg RNA/g ftt and 17.5 mg DNA/g ftt. Electron microscopy of tumor DNA showed it to be a linear unit, 20 Å in width and morphologically similar to that of normal liver and brain DNA. Paper chromatography of the DNA revealed a slightly different base composition than in normal brain or liver, but the guanine-cytosine content was about 42% in every case. Thermal denaturation and S values were comparable to that of normal liver.

70-1264 LIPID COMPOSITION OF ADENOVIRUS-INDUCED TUMOR. (E.) Ohmori, M. (Okayama U. Med. Sch., Japan) and Y. Kanemasa. Acta Med. Okayama 23(5):449-452, 1969.

Thin-layer and paper chromatography of lipid, prepared from adenovirus 12 (Huie strain)-induced tumors from 2-week-old Syrian hamsters, demonstrated a composition ratio of phospholipid components similar to other tumors, but with a slight reduction of the lecithin and sphingomyelin content. A glycolipid, probably a cerebroside, was present in fairly large quantities.

70-1265 PATHOGENESIS OF ONCOGENIC SIMIAN ADENOVIRUSES. VI. AN ULTRASTRUCTURAL INVESTIGATION OF SV30 REPLICATION. (E.) Slifkin, M. (U. Pittsburgh Sch. Med., Pa.), L. P. Merkow, M. Pardo and N. P. Rapoza. Exp. Molec. Path. 11(3):285-299, 1969.

About 1 hr. after infection of LLC-MK₂ monkey kidney cells with simian virus 30, 35% of the cells had virions adhering to the plasmalemma, and by 3 hr., there was some cytoplasmic 'bubbling' with membrane and non-membrane bound virus particles in the cytoplasm and nucleus; at 6 hr. prominent enlargement of the nucleus and nucleoli was observed. From 12-18 hr. virions were intermixed with focal condensations of the hypertrophied nucleolemma and there was the first appearance of newly-synthesized virus particles. These particles, at 18-20 hr., had a polygonal capsid with a slight-staining vesicular nucleoid or a large or smaller dense-type.

Virus particles were also contained in unusual tubular structures. Fluorescent antibody to T-antigen stained 80% of the cells at 12 hr., and there was a max. infectivity titer at 30 hr. Infected cells demonstrated increased annulate lamellae near the nucleus.

70-1266 DISTRIBUTION OF TUMOR ANTIGEN IN CELL FRACTIONS OF ADENOVIRUS 12-INDUCED TUMOR - ITS APPLICATION TO FLUORESCENT ANTIBODY TECHNIQUE. (E.) Okamoto, T. (Okayama U. Med. Sch. Cancer Inst., Japan). Acta Med. Okayama 23(1):13-20, 1969.

Homogenates of adenovirus 12 (Ad12)- induced tumors, and nuclear, mitochondrial, and microsomal fractions of these tumors all demonstrated complement-fixation with the sera from Ad12-tumor-bearing hamsters, the mitochondria and the microsomes having the highest titers. Direct staining with fluorescent antibodies from rabbits hyperimmunized with the microsomal fraction or indirect staining with tumor-bearing-hamster sera produced fluorescence in the cytoplasm of most tumor cells, especially adjacent to the cell membrane. Spot-like or entire fluorescence was seen in the nucleus of a few cells, and sera from normal hamsters produced no fluorescence.

70-1267 TRANSFORMATION OF HAMSTER CELLS IN VIVO AND IN VITRO BY AN ADENOVIRUS 4-SV40 HYBRID. (E.) Easton, J. M. (NCI, Bethesda, Md.), A. S. Rabson and R. A. Malmgren. Int. J. Cancer 5(1):15-20, 1970.

Adenovirus 4-SV40 hybrid induced both transformation of newborn hamster kidney cells in vitro and tumors in neonatally inoc. hamsters. Tumor was also produced by inj. of transformed cells into an irradiated weanling hamster. All tumors were fibrosarcomas similar to those induced in vivo by SV40 alone; no epithelial elements were seen. The 3 tumors were carried as serial transplants in hamsters, and each of the lines maintained a morphology slightly different from that of the other 2. Sera from hamsters carrying the tumors contained antibodies to T antigens induced in cell cultures of African green monkey kidney by Ad 4 and Ad 7, but not by Ad 12. This confirmed previous findings that genetic material from nononcogenic adenoviruses can be introduced into tumors and transformed cells by these hybrids. The cross-reaction with cells infected with Ad 7 provides additional evidence for a relationship between Ad 4 and the subgroup of oncogenic adenoviruses.

-1268 MENINGEAL TUMORS INDUCED IN CALVES WITH THE BOVINE CUTANEOUS PAPILLOMA VIRUS. (E.) Brobst, D. F. (Purdue U. Sch. Vet. Med., Lafayette, Ind.) and G. C. Dulac. Th. Vet. (Basel) 6(2):135-145, 1969.

Inoc. of 2-week-old calves with bovine papilloma virus (BPV), both in the meninges and intradermally, induced meningeal fibromas as early as 20 weeks in 11/14 and 6 fibropapillomas at the site of cutaneous inj; 6 of the calves with meningeal tumors failed to develop cutaneous lesions. Similar treatment of 8-mo.-old steers, which had been previously immunized with BPV resulted in meningeal tumors in 2/3 and no skin tumors. Mined fragments from a bovine cutaneous papilloma of 97 days duration were implanted in the anterior chamber of the eye and into the brain of 2-week-old calves, inducing brain tumors in 3/4 and surviving, but minimally cells proliferating, in the eye of 2. Inoc. of BPV in the meninges and abdominal viscera of 3 calves induced meningeal tumors in all, but abdominal tumors in only one. Meningeal tumors examined after 90 days extended into the brain along the course of the blood vessels, no metastases were observed and there was no evidence of virus or viral antigen in the tumors.

70-1269 ONCOGENICITY OF BOVINE PAPILLOMA VIRUS. (E.) Olson, C. (U. Wisconsin Coll. Vet. Sci., Madison), D. E. Gordon, M. G. Robl and K. P. Lee. Arch. Environ. Health (Chicago) 19(6):827-837, 1969.

Experimental induction, latent period, incidence and regression of fibropapillomas caused by bovine papilloma virus (BPV), in cattle and the appearance of the tumors in the light and electron microscope are described. The BPV stimulated growth in some epithelial cells, and reproduced in the nuclei of others that were degenerating. Histochemical studies on cellular enzymes were reviewed in relation to mechanism of action. Other neoplasms induced by the virus were discussed including, fibropapillomas of the genital mucosa, fibroblastic tumors of the brain and polypoid tumors of the urinary bladder in cattle, sarcoma-like tumors in the skin of horses, connective-tissue tumors in the hamster, and fibromas in C3H/eB mice.

70-1270 NEW ANTIGENS IN HAMSTER EMBRYO CELLS TRANSFORMED IN VITRO BY BOVINE PAPILLOMA EXTRACTS. (E.) Geraldes, A. (Gulbenkian Inst. Sci., Oeiras, Portugal). Nature (London) 226(5240):81-82, 1970.

Hamster and mouse embryo cells transformed in vitro by extracts of bovine papilloma (BPE) were studied by the indirect fluorescent antibody method. Specific fluorescence was observed exclusively in cells transformed by BPE when incubated with sera from hamsters bearing tumors induced by inoc. of BPE-transformed cells. Controls were negative. About 20% of hamster cells transformed by BPE showed specific fluorescence, which was always cytoplasmic and somewhat granular, whether transformed cells were hamster cells or

mouse cells. The observed fluorescence was probably related to the presence of cellular antigens and not to the presence of virus. The positive result with transformed mouse embryo cells indicated a viral rather than a cellular specificity of the new antigens.

70-1271 EFFECT OF COINFECTION WITH POLYOMA VIRUS ON MULTIPLICATION OF PICODNAVIRUSES X 14 OR H-1 IN RAT EMBRYO CELLS. (E.) Cocuzza, G. (U. Catania Inst. Microbiol., Italy) and A. Costarelli. Boll. Ist. Sieroter. Milan. 48(4): 301-304, 1969.

Rat embryo cells, coinfecting with polyoma virus (Py) and picodnaviruses X 14 or H-1, did not support multiplication of Py. The Py did not interfere with H-1 virus multiplication, but caused an increased titer of X 14 virus, more than 1 log unit in infectivity titer and a 3-fold increase in hemagglutination (HA) titer. The TCID₅₀:HA ratio was increased indicating the most important effect of coinfection with Py was on X 14 DNA synthesis.

70-1272 TRANSPLANTABILITY OF TUMORS INDUCED BY POLYOMA VIRUS. (Pol.) Chłap, Z. (Med. Acad. Inst. Anat.Path., Cracow, Poland), W. Jaszc and K. Kawecka-Jaszc. Pat. Pol. Suppl. 1:571-576, 1969.

Cell suspensions from a polyoma induced (in newborn Syrian hamster) subcutaneous sarcoma were inj. s.c. into groups of 1-4-mo.-old Syrian hamsters and after serial passage, caused sarcomas at site of inj. in 60/62 (96.7%) animals. Metastases to lungs were also noted in 2 hamsters. Rate of tumor growth increased with each successive passage and latency decreased from 15-20 days in the first 5 passages to 7-8 days in passage 8-10 indicating increase in malignancy with successive passage. Progressive de-differentiation and marked increase in mitotic activity (10-fold in 7th passage) were also noted. The tumor cells were passaged *in vitro*, maintained their neoplastic characteristics, and were capable of producing tumors at site of inj. when inoc. into hamsters. Two types of tumor cells were observed in histological preparations and *in vitro* cell cultures and described in detail.

70-1273 KINETICS OF MEMBRANE ANTIGEN IN THE HAMSTER POLYOMA VIRUS SYSTEM. (Fr.) Meyer, G. (Reg. Cancer Res. Ctr., Marseille, France), F. Birg and H. Bonneau. C. R. Soc. Biol. [D] (Paris). 268(23):2848-2849, 1969.

When a culture of BHK 21/13 cells was infected with hamster polyoma virus (100 plaque-forming

U/cell), membrane antigen was demonstrable in some cells as early as the sixth hour after infection, reached max. (75% of the cells) at the seventeenth hour, then decreased rapidly after the nineteenth hour to reach a low of 6-7% positive cells by the second or third day. This low was maintained, without further decrease, until cellular degeneration set in, at about the twelfth day. Only 5%-6% of the cells involved underwent a complete transformation, a phenomenon which had been observed previously in studies of nuclear immunofluorescence antigen.

70-1274 TRANSFORMATION OF ODONTOGENIC EPITHELIUM BY POLYOMA VIRUS *IN VITRO*. (E.) Main, J. H. P. (U. Edinburgh). J. Dent. Res. 48(5):738-744, 1969.

Mandibular and maxillary incisor tooth germs, taken from 13-14-day-old C3H/BI mouse embryos, were placed in a polyoma virus suspension or a control kidney homogenate for 1 hour, then cultured on gelatin sponges. The uninfected tooth cells differentiated from the cap stage to the bell stage after 7 days, underwent necrosis by the second week, and by the third week were spread and clumped over the sponge surface. In the infected culture, necrosis was extensive by 7 days and no differentiation had occurred; by 21 days the cells were larger than controls, pleomorphic, and in cords and clumps with viral inclusion bodies and mitotic figures. Transplantation of control cells s.c. in histocompatible mice resulted in the growth of normal incisor teeth, whereas virus-infected cells produced small masses of proliferating epithelial cells in about 25% of the mice, similar to those seen in the cultures.

70-1275 ENHANCEMENT OF HAEMAGGLUTININ PRODUCTION IN POLYOMA VIRUS-INFECTED CANDIDA BY A DEFINED MEDIUM AND URETHAN. (E.) Kovács, E. (U. Toronto, Canada) and G. Kolompár. Experientia 26(3):301-303, 1970.

The hemagglutinin production of *Candida albicans* inoc. with polyoma virus (PyV) was measured; PyV went through 30 passages in yeast before being used as inoculum. A 0.2 ml cell homogenate containing 2048 hemagglutinating units was added to 0.3 ml log phase yeast culture (10⁶ cells). Urethan (50 mg) was added to some systems. Experiments were carried out for 4 or 24 hours in natural or defined medium, the latter containing 0.15 M sucrose. More cell-associated hemagglutinins were found with defined medium. PyV was stimulated by urethan; U-stimulation was observed only in defined medium + sucrose, lacking macromolecules.

70-1276 EPIDEMIOLOGIC STUDIES OF LATENT VIRUS INFECTIONS IN CAPTIVE MONKEYS AND BABOONS. I. OVERALL PLANS AND VIRUS ISOLATIONS WITH SPECIAL REFERENCE TO SV40 AND FOAMY VIRUSES. (E.) Hsiung, G. D. (VA Hosp., West Haven, Conn.), T. Atoyan and C. W. Lee. Amer. J. Epidemiol. 89(4):464-471, 1969.

From February 1966 through April 1967, kidney cell suspensions from 253 rhesus and 216 green monkeys were examined and viruses were found in more than half with no seasonal variation. Simian virus (SV40) occurred more in the green monkey (74/117), and foamy viruses were more common in rhesus monkeys (89/119). There were mixed infections in 12 rhesus and 9 green monkeys. It seemed that SV40 infection in green monkeys was most prevalent when the monkeys were held in the laboratory for 50-80 days; a higher percentage of rhesus monkeys with foamy virus had been held in the lab less than 50 days. Only 2/13 baboon kidney cell cultures had virus. No SV5 was found in any study.

70-1277 DEVELOPMENT OF SV40 COAT PROTEIN ANTIGEN IN NON PERMISSIVE NUCLEI IN HETEROKARYO-CYTES. (E.) Steplewski, Z. (Wistar Inst. Anat. Biol., Philadelphia, Pa.) and H. Koprowski. Exp. Cell Res. 57(2-3):433-440, 1969.

Human W 98Va C cells, transformed by SV40, were fused with African green monkey kidney (AGMK) cells and infected with 100 PFU of Simian virus 40 (SV40)/cell 24 hr. later. After 46 hour, immunofluorescent staining for viral coat protein (VP) showed equal intensity in both nuclei of a binucleated heterokaryon cell. Similar results were obtained using AGMK cells and mouse or hamster embryo fibroblasts, Nil-2 line of hamster embryo fibroblasts, or 2A-1 line of GMK-EVa cells. The presence of one permissive AGMK nucleus was sufficient to affect all the other nuclei. Canavanine (32 µg/ml) placed in the heterokaryon culture before infection prevented appearance of the VP-antigen. When placed in the medium of Nil-2 cells before fusion with infected AGMK cells, canavanine gave variable results depending on the proportion of the 2 types of nuclei in the heterokaryon cell. Parallel results were obtained when 0.1 µg/ml actinomycin D was used.

70-1278 MONKEY-MOUSE HYBRID CELL LINES CONTAINING THE SV40 GENOME IN A PARTIALLY RE-PRESSED STATE. (E.) Kit, S. (Baylor Coll. Med., Houston, Tex.), K. Nakajima, T. Kurimura, D. R. Dubbs and R. Cassingena. Int. J. Cancer 5(1):1-14, 1970.

The characteristics of somatic hybrid cell lines derived from mixed cultures of SV40-transformed mouse kidney (mKS-BU100) cells and an established line of African green monkey kidney (CV-1) cells is described. The monkey-mouse hybrid cells contained the SV40 T-antigen and transplantation antigen. Hybrid cells were resistant to super-

infection with SV40 DNA. Thymidine kinase (TK), deoxycytidylate (dCMP) deaminase and tRNA methylase activities were found in the hybrid cells. TK was partially purified from hybrid cells and the kinetic properties of the enzyme compared with those from parental cell lines and SV40-infected monkey kidney cells. The enzyme from hybrid cells resembled TK of CV-1 cells; this suggested that a monkey chromosome with a gene for TK was still present in hybrid cells. The SV40 function producing an altered TK was repressed in the hybrid as well as in mKS-BU100 cells. The tRNA methylase activities of the hybrid lines were of the same order of magnitude as those of the SV40-transformed cell lines. The dCMP deaminase activity of mK-CV¹ clone 4 was characteristic of SV40-transformed mouse kidney cells, but that of early passage mK-CV¹¹¹ clone 1 cells was very high and characteristic of CV-1 monkey kidney cells. The levels decreased during passage of mK-CV¹¹¹ clone 1 cells to a value about 2 times that of parental mKS-BU100 cells; this suggested that one of the monkey chromosomes of mK-CV¹¹¹ clone 1 cells had at least one active gene for dCMP deaminase.

70-1279 ISOLATION OF DOUBLE LYSOGENS FROM 3T3 CELLS TRANSFORMED BY PLAQUE MORPHOLOGY MUTANTS OF SV40. (E.) Dubbs, D. R. (Baylor Coll. Med., Houston, Tex.) and S. Kit. Proc. Nat. Acad. Sci. USA 65(3):536-543, 1970.

Simian virus 40 (SV40) rescued from 3T3 lines transformed independently by fuzzy (f) plaque strain SV40(mKS-U4) and small-clear (sc) plaque strain, SV40(mKS-U88), resembled the virus employed to initiate transformation. Both plaque types could be rescued when a mixture of the 2 viruses was used for transformation. Two clonal lines, after fusion with CV-1 cells, gave both plaque types of infectious centers; a third clonal line, 3T3(4-88)G-1, yielded f and sc plaque types of infectious centers and large-clear (1c) infectious centers resembling wild-type SV40 clone 307L. Two secondary and 14 tertiary clones of 3T3(4-88)G-1 were isolated; these all gave f plaque type and clear infectious centers after fusion with CV-1 cells. When these infectious centers were picked and replated on CV-1 cells, the f and sc plaque types of SV40 plus a 1c plaque type similar to parental SV40, were isolated.

70-1280 HYBRIDIZATION BETWEEN SV40 DNA AND CELLULAR DNA'S. (E.) Aloni, Y. (Weizmann Inst. Sci., Rehovot, Israel), E. Winocour, L. Sachs and J. Torton. J. Molec. Biol. 44(2):333-345, 1969.

Simian virus 40 (SV40) DNA was found to hybridize with BS-C-1 monkey-cell DNA even after fractionation by a heat procedure, methylated-alkaline-sieve chromatography, equilibrium centrifugation in cesium chloride (CSCI) solution supplemented with ethidium bromide, or band

sedimentation in neutral or alkaline CsCl solution. This was not true of polyoma virus and mouse-cell DNA. All particles of SV40 DNA, separated by density gradient centrifugation, hybridized to a significant extent with DNA from monkey cells. Labeling of monkey cells with ^{14}C -bromodeoxyuridine before infection with SV40 and labeling after with ^3H -thymidine showed no evidence of encapsulation of host DNA. About 7-9% of the SV40 DNA was found to hybridize with that of monkey cells, a smaller amount with DNA from 3T3 mouse cells, and not at all with chicken or E. coli DNA.

- 70-1281 INDUCTION IN HAMSTERS OF VARIOUS CARCINOMAS AND SARCOMAS BY IN-VITRO SV40-TRANSFORMED HOMOLOGOUS EMBRYONIC SKIN AND SUBCUTANEOUS TISSUE CELLS. ROLE OF TARGET CELLS IN DETERMINING TUMOR MORPHOLOGY. (E.) Diamandopoulos, G. T. (Harvard Med. Sch., Boston, Mass.) and M. F. Dalton-Tucker. Amer. J. Path. 56(1):59-77, 1969.

Golden Syrian hamster embryo cells were cultured and infected with simian virus 40, strain VA 45-54. Infected cultures showed an increase in cell population, more mitotic figures, some multinucleate giant cells and acidified the medium more than controls. After 1-3 mo., infected and normal cells (0.5 ml containing about 5×10^5 cells) were implanted subepithelially into both cheek pouches of 21-day-old male Syrian hamsters, and in some animals i.m. and s.c. Tumors induced by infected cells derived from one litter, were seen at all 3 sites - cheek pouch, i.m. and s.c. - and 3/17 gave rise to both epidermoid carcinomas and sarcomas, while 14 induced only histologic varieties of sarcomas. Infected cells from a second litter induced poorly-to-well-differentiated sarcomas in all cases and only one line produced adenocarcinomas in addition. Another induced a sarcomatous tumor which formed rosettes.

- 70-1282 EARLY IN-VITRO SV40-MEDIATED MORPHOLOGIC TRANSFORMATION OF PRIMARY HAMSTER CELLS. ITS CORRELATION WITH THE DEVELOPMENT OF THE ONCOGENIC STATE. (E.) Diamandopoulos, G. T. (Harvard Med. Sch., Boston, Mass.), M. F. Dalton-Tucker and J. van der Noordaa. Amer. J. Path. 57(2):199-213, 1969.

Golden Syrian hamster embryo cells were noted to undergo morphologic transformation as early as 2-3 days after infection with simian virus 40, (SV40) strain VA 45-54. Cells from infected cultures derived from 1 litter, when inj. intra-epithelially into the cheek pouches of male 21-day-old Syrian hamsters 1-6 days after virus inoc., produced tumors in only 20%. The tumors grew slowly and reached a max. size of 1-2 cm at the end of 4 mo. growth in vivo. Cells from another litter, after culturing for 1 mo. after infection,

induced tumors in 40% of the hamsters, and after culturing for 2-3 mo., in 80-90% of the animals. These tumors grew faster and reached a max. dimension of 3-5 cm in 4 mo. All tumors were well-to-poorly differentiated sarcomas and were positive for SV40 T antigen.

- 70-1283 SV40-SPECIFIC RNA IN THE NUCLEUS AND POLYRIBOSOMES OF TRANSFORMED CELLS. (E.) Lindberg, U. (Albert Einstein Coll. Med., New York, N. Y.) and J. E. Darnell. Proc. Nat. Acad. Sci. USA 65(4):1089-1096, 1970.

Heterogeneous nuclear RNA and polysomal RNA of cells transformed by the oncogenic virus SV40 are analyzed. Nuclear molecules containing virus-specific sequences were considerably longer than presumed virus-specific mRNA molecules from cytoplasmic polyribosomes. Results showed that there were nuclear molecules $>4 \times 10^6$ and polysomal molecules $<1.7 \times 10^6$ that contained RNA sequences complementary to SV40 DNA. These findings suggest the possibility that cytoplasmic mRNA is derived by the specific cleavage of larger nuclear RNA.

- 70-1284 CYTOCHEMICAL STUDIES OF HUMAN THYROID CELLS INFECTED WITH SV40. (Pol.) Karwacka, H. and L. Jabłoński (Med. Acad., Lublin, Poland). Med. Dosw. Mikrobiol. 22(1):71-74, 1970.

Five-day-old thyroid cell cultures were infected with 100 TCID₅₀ of SV40 and examined 48 and 96 hours later. Early morphological changes (seen in 25% of cells) included enlargement of nuclei (frequently to twice normal size), appearance of polynuclear (2-3 nuclei) cells and changes in the shape of nucleoli. After 96 hours 75% of cells were degenerated. Determinations of activity and distribution of ATP ase and nucleotidase revealed that activity of both enzymes was either markedly reduced or absent in infected cells, especially those showing morphological changes. The distribution of enzymes within these cells differed from that seen in control cells.

- 70-1285 TRANSFORMATION BY SV40 VIRUS OF ADULT GOLDEN HAMSTER KIDNEY CELLS CULTIVATED IN VITRO. (Rum.) Şahnazarov, N. (Nicolau Inst. Inframicrobiol., Bucharest), M. Nachtigal, L. H. Graffe and Ş. Ionescu-Homoriceanu. Stud. Cercet. Inframicrobiol. 20(6):433-460, 1969.

Renal cells of the adult male golden hamster inoculated in vitro with the simian virus (SV40) exhibited alterations in a number of parameters. Modification of growth and morphology appeared early (9-12 days after inoc.) marked by foci of multiple stratification and cells with abnormal nuclei. Presence of the neoantigen T-SV40 in

the inoc. cell line was evidence of the specificity of the transformation. Cytogenetic analysis of different passages *in vitro* indicated karyotypic instability although most variant cells had chromosome numbers close to the diploid value, the deviations becoming restricted by the twentieth passage to deletion of the X chromosome, and occasionally the presence of an extra D chromosome. The line acquired oncogenic potential on day 225 after inoc. with SV40. The transformed cells were partially susceptible to infection by herpes simplex virus.

70-1286 THE PATTERN OF PROTEIN SYNTHESIS IN SV40-INFECTED CV-1 CELLS. (E.) Fischer, H. (German Cancer Res. Ctr. Inst. Virus Res., Heidelberg) and K. Munk. Int. J. Cancer 5(1):21-27, 1970.

The time sequence of induced proteins after SV40 infection was studied by polyacrylamide gel electrophoresis; confluent CV-1 cell cultures were infected with SV40 at a multiplicity of 20 PFU/cell. The alteration of protein pattern was studied in stained gels of protein preparations and in gels of protein preparations after pulse labelling cells with ^{14}C -amino acids. The precipitated protein pattern was altered after infection in correlation with changes in pattern of incorporated isotopes. New bands and increases in bands present in the control cultures were seen. Following urea treatment, the particulate protein pattern showed 3 new peaks at 15 hours after infection. The most significant alterations, compared to uninfected CV-1 cells, were at 32 hours after infection. Three complexes, peaks 18, 10-13 and 14-17, and peak 23 increased at this time. Protein synthetic activity in these areas was confirmed by electrophoresis of pulse-labeled proteins.

70-1287 COMPARATIVE STUDIES ON THE CARBOHYDRATE-CONTAINING MEMBRANE COMPONENTS OF NORMAL AND VIRUS-TRANSFORMED MOUSE FIBROBLASTS. I. GLUCOSAMINE-LABELING PATTERNS IN 3T3, SPONTANEOUSLY TRANSFORMED 3T3, AND SV-40-TRANSFORMED 3T3 CELLS. (E.) Wu, H. C. (California Inst. Technol., Pasadena), E. Meezan, P. H. Black and J. W. Robbins. Biochemistry (Wash.) 8(6): 509-517, 1969.

Cell line 3T3 and SV40 virus-transformed 3T3 cells were labeled with ^3H - and ^{14}C -glucosamine; the cells were then harvested and mixed as follows: ^3H -SV40-3T3 and ^{14}C -3T3, and ^3H -3T3 and ^{14}C -SV40-3T3. After separation into the ^3H to ^{14}C ratios were also determined for sialic acid, galactosamine and glucosamine isolated from each fraction. Analysis of the relative composition of membrane glycoproteins and lipids showed a much lower sialic acid and galactosamine content, and a reciprocal increase in the relative content of glucosamine in SV40-3T3 as compared with 3T3. These differences were found in all particulate fractions, but not in

the nucleotide sugar fraction; the changes in membrane carbohydrate composition in virus-transformed cells could thus not be attributed to a lack of particular nucleotide sugar precursors. Measurements of the absolute amounts of neutral and amino sugars present in the particulate fractions of 3T3 and SV40-3T3 showed a marked decrease in both in SV40-3T3. Measurements of sugar contents in spontaneously-transformed 3T3 showed decreased amounts of both neutral and amino sugars, with levels intermediate between those present in 3T3 and SV40-3T3.

70-1288 RESCUE OF SIMIAN VIRUS 40 FROM CELL LINES TRANSFORMED AT HIGH AND AT LOW INPUT MULTIPLICITIES BY UNIRRADIATED OR ULTRAVIOLET-IRRADIATED VIRUS. (E.) Kit, S. (Baylor Coll. Med., Houston, Tex.) and M. Brown. J. Virol. 4(3):226-230, 1969.

Mouse kidney-cell cultures from 10-14-day-old Swiss mice were transformed by infection with unirradiated simian virus 40 (SV40 - input multiplicities of 200-1006 PFU/cell), or ultraviolet (UV)-irradiated SV40 (8.0 to 4×10^{-5} PFU/cell). All the transformed cells in the culture were used to establish cell lines. Recovery of virus was accomplished by incubation of the transformed cells with cultures of CV-1 green monkey kidney cells suspended in a medium containing UV-inactivated Sendai virus. All lines transformed by unirradiated virus, even at a multiplicity of .06, gave good yields of SV40, but the incidence of successful rescue and frequency of induction did not depend on multiplicity of infection. However, the cells transformed by irradiated virus with input multiplicities of 8 and 2, PFU gave poor yields, and the lower input multiplicities gave none.

70-1289 HETEROGENEOUS DNA OF SIMIAN VIRUS 40. (E.) Yoshiike, K. (Nat. Inst. Health, Kamiosaki, Tokyo) and A. Furuno. Fed. Proc. 28(6):1899-1903, 1969.

The biological properties of defective deletion mutants of simian virus 40 (SV40) and the nature of plaque-forming deletion mutants are compared to the wild-type SV40. The deletion mutants, which formed a major proportion of the virions resulting from serial undiluted passages, contained a slightly shorter heterogeneous DNA and some produced abortive infections in green monkey kidney cells. These mutants had a stable genetic character, produced smaller plaques which appeared later and produced heterogeneous DNA at a higher efficiency. Tumorigenicity was parallel to T-antigen-forming ability.

70-1290 ONCOGENESIS OF THE YABA MONKEY TUMOR VIRUS. (E.) Tsuru, K. (Kobe U. Sch. Med., Hyogo, Japan). Jap. J. Derm. (Ser. B) 78(3):463-469, 1968.

LLCMK2 cells, derived from rhesus monkey kidney, were inoc. with Yaba Monkey Tumor Virus (YMT-V) from rhesus monkey testicular tumor. About 3.2% of the cells had intracytoplasmic inclusions similar to "B" type pox virus. Staining with fluorescein-labeled anti-YMT-V monkey sera produced fluorescence at the site of the inclusions. Cross reaction between this antibody and other pox viruses (cowpox, vaccinia, Shope fibroma-V) was observed. Labeling of the cells by incubating with ^3H -thymidine and applying autoradiographic technics, showed that DNA synthesis in inclusion-bearing cell was suppressed. Similar results were obtained with tumors induced in vivo by YMT-V in a cynomolgus, a rhesus and a Japanese monkey.

70-1291 IN VITRO TITRATION OF SHOPE FIBROMA VIRUS. (Sp.) Suarez, H. G. (Nat. Acad. Med. Inst. Hemat. Res., Buenos Aires, Argentina). Medicina (B. Air.) 28(Suppl. 1): 165-168, 1968.

A method is described for titrating Shope fibroma virus in vitro, using RK 13 cells and Eagle's medium with 4 x the usual quantity of amino acids and 8 x the usual quantity of vitamins, + calf, fetal bovine or rabbit serum. The final titer, using these three sera, was $6.2-6.6 \times 10^6$ plaque-forming units/ml. Substituting horse serum resulted in 30% inhibition of the number of plaques obtained. However, a serum neutralization test, using another batch of horse serum in conc. of 5%-50%, failed to inhibit plaque formation at any conc. level, excluding the possibility of any specific antiviral activity on the part of horse serum. It is suggested that the inhibition observed in the first trial may have been due to cross antigenicity between the Shope virus and some virus of the pox group which was present in the serum of the non-immunized animal which was used as a donor.

70-1292 VIRUS-LIKE NUCLEAR DEGENERATION IN MALIGNANT MELANOMA. (E.) Hairstone, M. A. (U. Tehran Pahlavi Hosp. Cancer Res. Inst., Iran) and W. C. Cooper. Acta Med. Iran. 11(1-2): 1-8, 1968.

Electron microscopy of a malignant melanoma from the right eye of a 37-yr.-old white female revealed oval, round or channeled masses within the nuclei of pigmented cells. The particles were 260 - 300 m μ in size, were surrounded by a double membrane, and were composed of many vesicular variations. Some contained a central nucleoid, which was less dense or elliptical in others. The particles could not be grown in tissue culture, and no determination of nucleic acid content has been made. Similar inclusions were not seen in 4 other malignant melanomas examined.

70-1293 VIRUS IN CELL CULTURE DERIVED FROM HUMAN TUMOUR PATIENTS. (E.) Todaro,

G. J. (NCI, Bethesda, Md.), V. Zeve and S. A. Aaronson. Nature (London) 226(5250):1047-1049, 1970.

In 3/56 cell strains studied, incorporation of radioactively-labeled uridine into particles in the supernatant fluid was found by sucrose gradient sedimentation, indicative of an RNA-containing virus; these were in 3/22 strains from tumor pts., while 0/34 strains from non-tumor pts. showed evidence of virus. The positive strains were strain 8387 from a fibrosarcoma, strain F230 from a breast carcinoma and strain L37 from a fibroblast culture of a pt. with acute lymphocytic leukemia. Each of the 3 virus-containing cell lines grew readily in culture, and further studies may indicate whether the viruses are etiologically involved in human cancer or are passengers only.

70-1294 VIRUS FORMATION IN HeLa/INO CELLS CULTURED IN VITRO STARTING ON DNA FROM LYMPH NODES OF HODGKIN'S DISEASE. (E.) Valladares, Y. (City Univ. Nat. Inst. Oncol., Madrid), Y. Alvarez, E. Tabarés and T. Pintado. Arch. Geschwulstforsch. 34(4):289-296, 1969.

DNA (7.5 $\mu\text{g/ml}$ growth medium) from a lymph node of a female pt. with the paraneoplastic type of Hodgkin's disease was inoc. into several cell strains maintained in vitro. In the HeLa/INO cell cultures, the DNA produced cytopathic effects and clonal clusters of transformed cells. Growth medium from passage 30 gave a positive virus titration in mouse embryo cells (3.16×10^6 infective particles/ml), and a high mortality, but no specific lesions in newborn mice. These particles with viral properties were obtained, although no vegetative virus pre-exists.

70-1295 VIRUS-LIKE PARTICLES IN BOWEN'S DISEASE. (E.) Nordquist, R. E. (U. Oklahoma Sch. Med., Oklahoma City), R. L. Olson, M. A. Everett and P. T. Condit. Cancer Res. 30(2): 288-293, 1970.

Electron microscopic studies of tissue from 6/7 lesions of Bowen's disease, revealed the presence of virus-like cytoplasmic particles (about 800-1100 Å in diameter) in the basal and spinous layers. The particles appeared to be budding from the plasma membrane or a membrane-like surface, after which they were extruded into the intercellular space. The extracytoplasmic particle consisted of alternate light and dense layers, with a less dense nucleoid containing 2 or more electron dense particles. No similar virus-like particles were seen in 44 samples of normal skin or 12 samples from other epidermal diseases.

70-1296 SPONTANEOUS NEOPLASTIC TRANSFORMATION OF GERM-FREE RAT EMBRYO CELL CULTURE.

(E.) Sharon, N. (U. Notre Dame, Ind.) and M. Pollard. Cancer Res. 29(8):1523-1526, 1969.

The use of rat and rat embryo cell cultures as a virus-free model system for the study of spontaneous neoplastic transformation is described. Cells from normal germ-free Wistar rat embryos were propagated *in vitro* and showed morphologic conversion to epithelium-like cells on the eighth passage. The nineteenth passage *in vitro* of the converted cells induced progressively growing local fibrosarcomas in newborn rats; tumors were not transplantable to additional rats. Sprague-Dawley rats were more receptive to the transformed Wistar cells than Wistar or Fischer rats. No detectable virus particles or viral antigens were found in the inoc. rats, the normal and transformed cell cultures or the tumors. The results suggest that transformation of cells *in vitro* and their ability to initiate tumors can occur without the involvement of a detectable exotic microbial factor.

0-1297 VIRUS-LIKE PARTICLES IN MURINE EPENDYMOBLASTOMA. (E.) Rubin, R. (Albert Einstein Coll. Med., Bronx, N. Y.), R. P. Ames, C. J. Sutton and H. M. Zimmerman. J. Neuropath. exp. Neurol. 28(3):371-387, 1969.

Electron microscopy of tissue from brain tumors, induced in 2-3-mo.-old C57B1/6 mice by intracerebral inj. of methylcholanthrene-induced tumors, revealed the presence of aggregates of 0-100 virus-like particles in the cytoplasm. These particles were noted to be in the form of a doughnut-shaped ring, have a variable central core, not to be associated with any intracellular organelles, and to be associated with dense bodies of 3 morphological types. A second virus-like particle was noted at the cell surface and extracellularly. On a structural basis, this virus may be a member of the family *Thylaxoviridae*.

0-1298 ON PLASMOCYTOMA ONCOGENESIS OF MICE. III. ANNULATE LAMELLAE WITH UNUSUAL MORPHOLOGY IN A PLASMOCYTOID NEOPLASIA OF MICE (HAPA TUMOR). (E.) Grieshaber, E. (U. Zurich stopath. Inst., Switzerland), G. Pedio and J. Rüttner. Path. Microbiol. (Basel) 33(1):1-13, 1969.

Spindle-cell mesenteric neoplasm, induced with mineral oil in BALB/c mice, showed young poorly differentiated cells and immature plasma cell types after the third transplant generation. Characteristic annulate lamellae were seen in 5% of both types. In a polar location to the Golgi complex and related to the rough endoplasmic reticulum, unusual annulate lamellae were found with a great number of closely arranged parallel layers and short cisternae, whose pores were filled with an amorphous substance. Filament-like structures were seen between pores of neighboring layers and ribosomes. Virus-like

type C particles were localized in the region of the annulate lamellae and also extracellularly.

70-1299 SQUIRREL VIRUSES. (E.) Vizoso, A. D. (Microbiol. Res. Establ., Salisbury, Wiltshire, England). Proc. Roy. Soc. Med. 63(4):341-344, 1970.

Agents obtained from native red squirrels of Britain, and designated RS3/2 (from a healthy animal), RS6 and RS21, were studied. BHK cells transformed by RS6 induced sarcomas when inoc. into suckling Syrian hamsters; the tumors were transplantable in adult hamsters, produced hemagglutinins and also virus infectious for normal BHK cells. A colony of transformed cells, from RS6, showed a decrease in the number of cells with eosinophilic inclusion bodies from 90% to about 10% in 18 passages. RS21 was obtained from tumors in a red squirrel. All of the agents caused cell transformation and inoculates of the transformed cells produced tumors from which virus was recovered. Strains collected from the diseased animals appeared very similar in all respects to those from the apparently healthy animal, but the virus titer from the diseased animals was appreciably higher, by 6-7 logs. Some characteristics of the isolates suggest the presence of a virus of the parainfluenza group.

70-1300 CORRELATION BETWEEN "CRISIS" AND VIRUS PRODUCTION IN SV40 TRANSFORMED HUMAN AMNION CULTURES. (E.) Fogh, J. (Sloan-Kettering Inst., Rye, N. Y.), J. D. Loveless and E. V. Gaffney. Fed. Proc. 28(2):297, 1969.

70-1301 LEUKEMOID REACTIONS IN GERM-FREE RATS WITH ROUS SARCOMA VIRUS (RSV)-INDUCED SARCOMAS. (E.) Pollard, M. (U. Notre Dame, Ind.) and M. Kajima. Fed. Proc. 28(2):297, 1969.

70-1302 EARLY APPEARANCE OF GROSS LEUKEMIA FOLLOWING INTRATHYMIC INJECTION. (E.) Mariani, T. (Variety Club Heart Hosps. Pediat. Res. Labs., Minneapolis, Minn.). Fed. Proc. 28(2):297, 1969.

70-1303 VIRUS-INDUCED SARCOMA OF MICE: INHIBITION BY AN RNA INDUCER OF INTERFERON. (E.) Sarma, P. S. (NIH, Bethesda, Md.), G. Shiu, R. Neubauer, S. Baron and R. J. Huebner. Fed. Proc. 28(2):297, 1969.

70-1304 VIRUS KINETICS IN MURINE SARCOMA. (E.) Imahori, S. (New England Deaconess Hosp. Cancer Res. Inst., Boston, Mass.). Fed. Proc. 28(2):297, 1969.

70-1305 HOST RANGE VARIANTS OF MURINE LEUKEMIA VIRUS. (E.) Meier, H. (Jackson Lab., Bar Harbor, Maine), D. D. Myers and R. J. Huebner. Fed. Proc. 28(2):298, 1969.

70-1306 INTRACELLULAR DISTRIBUTION OF NUCLEASES AND NUCLEIC ACIDS IN FRIEND LEUKEMIA MOUSE SPLEEN. (E.) Chakrabarty, A. (Albert Einstein Med. Ctr., Philadelphia, Pa.), W. Ceglowski and H. Friedman. Fed. Proc. 28(2):298, 1969.

70-1307 ATTEMPTS AT UNMASKING THE RSV IN MONKEYS TUMOR. (E.) Kung, T. (New York U. Med. Ctr. Inst. Rehab. Med., N. Y.), M. Lyons, I. Munroe and B. Bates. Fed. Proc. 28(2):298, 1969.

70-1308 EFFECTS OF IMMUNIZATION WITH SIMIAN ADENOVIRUS SA-7 ON THE TRANSPLANTABILITY OF SA-7 TUMOR CELLS. (E.) Casto, B. C. (AMA Inst. Biomed. Res., Chicago, Ill.), G. L. Van Hoosier, Jr. and J. J. Trentin. Fed. Proc. 28(2):298, 1969.

70-1309 PERSISTENCE OF GROSS LEUKEMIA VIRUS INFECTION IN VITRO. (E.) Imagawa, D. T. (U. California Med. Sch. Harbor Gen. Hosp., Torrance) and M. Nakai. Fed. Proc. 28(2):298, 1969.

70-1310 INHIBITION OF ADENOVIRUS-12 ONCOGENESIS IN MALE AND FEMALE HAMSTERS. (E.) Li, C. P. (NIH, Bethesda, Md.), B. Prescott and E. C. Martino. Fed. Proc. 28(2):313, 1969.

70-1311 MORPHOLOGIC AND FUNCTIONAL EFFECTS OF POLYOMA VIRUS ON MOUSE LYMPHATIC TISSUES. (E.) Proffitt, M. R. (U. Tennessee, Knoxville) and C. C. Congdon. Fed. Proc. 28(2):313, 1969.

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70-1313 VIRUS-SPECIFIC ANTIGENS IN HAMSTER CELLS TRANSFORMED BY ROUS SARCOMA VIRUS. (E.) Fleissner, E. (Sloan-Kettering Inst., New York, N. Y.). Fed. Proc. 28(2):313, 1969.

70-1314 CONTINUOUS VIRAL REPLICATION AND MALIGNANT CELLULAR TRANSFORMATION IN

RAT EMBRYO CELLS INFECTED WITH FINKEL'S OSTEO-SARCOMA VIRUS. (E.) Rhim, J. S. (Microbiol. Assoc., Inc., Bethesda, Md.), R. J. Huebner, W. T. Lane and H. C. Turner. Fed. Proc. 28(2):313, 1969.

70-1315 INACTIVATION RATES OF THE INFECTIVITY AND TUMORIGENICITY OF THE ONCOGENIC SIMIAN ADENOVIRUS SA-7. (E.) Van Hoosier, G. L., Jr. (Baylor U. Coll. Med., Houston, Tex.), B. C. Casto and J. J. Trentin. Fed. Proc. 28(2):313, 1969.

70-1316 ALTERATIONS IN BIOLOGIC CHARACTERISTICS OF VIRUS INDUCED HAMSTER TUMOR CELLS BY NUCLEIC ACID. (E.) Goldner, H. (Albert Einstein Med. Ctr. Korman Res. Labs., Philadelphia, Pa.) and D. R. Meranze. Fed. Proc. 28(2):314, 1969.

70-1317 TWO DISTINCT TYPES OF SV40 TRANSFORMED HUMAN AMNION CELLS. (E.) Gaffney, E. V. (Sloan-Kettering Inst., Rye, N. Y.), L. Ramos and J. Fogh. Fed. Proc. 28(2):314, 1969.

70-1318 RAUSCHER LEUKEMIA VIRUS-INDUCED IMMUNOSUPPRESSION OF SPLEEN CELLS CULTURED IN MILLIPORE DIFFUSION CHAMBERS. (E.) Borella, L. (St. Jude Child. Res. Hosp., Memphis, Tenn.). Fed. Proc. 28(2):314, 1969.

70-1319 ALTERED tRNA METHYLASE ACTIVITIES IN A GA VIRAL INDUCED CHICK LIVER TUMOR. (E.) Hacker, B. (Merck Inst. Therap. Res., Rahway, N. J.), L. R. Mandel and T. Maag. Fed. Proc. 28(2):350, 1969.

70-1320 AN ENDONUCLEASE ASSOCIATED WITH ADENOVIRUS TYPES 2 AND 12. (E.) Burlingham, B. T. (Rockefeller U., New York, N. Y.) and W. Doerfler. Fed. Proc. 28(2):434, 1969.

70-1321 ROLE OF INTERFERON IN SUPPRESSION BY STATOLON OF ESTABLISHED FRIEND VIRUS INFECTION IN DBA/2 MICE. (E.) Wheelock, E. F. (Case Western Res. U., Cleveland, Ohio) and N. L. Caroline. Fed. Proc. 28(2):503, 1969.

70-1322 SURFACE ANTIGENS IN CELLS TRANSFORMED BY PAPOVAVIRUS SV40. (E.) Tevethia, S. S. (Baylor U. Coll. Med., Houston, Tex.), R. N. Lausch, S. Layne and F. Rapp. Fed. Proc. 28(2):567, 1969.

70-1323 SURFACE CHANGES IN SV40-TRANSFORMED AND TUMOR CELLS. (E.) Defendi, V. (Wistar Inst. Anat. Biol., Philadelphia, Pa.) and P. Hayry. Fed. Proc. 28(2):567, 1969.

70-1324 ANTIGEN AND BIOCHEMICAL CHANGES IN
MEMBRANES OF VIRUS-TRANSFORMED CELLS.

(E.) Black, P. H. (Massachusetts Gen. Hosp.,
Boston), H. Wu, E. Meezan, H. T. Robertson and
P. W. Robbins. Fed. Proc. 28(2):567, 1969.

70-1325 APPEARANCE OF FORSSMAN ANTIGEN ON THE
CELL SURFACE FOLLOWING TRANSFORMATION
BY VIRUSES. (E.) O'Neill, C. H. (Massachusetts
Gen. Hosp. Biochem. Res. Lab., Boston). Fed.
Proc. 28(2):568, 1969.

70-1326 DIFFERENCES IN THE BIOCHEMICAL
ARCHITECTURES OF SURFACE MEMBRANES OF
NORMAL AND VIRALLY TRANSFORMED CELLS. (E.)
Muller, M. M. (Princeton U., N. J.). Fed. Proc.
28(2):568, 1969.

70-1327 SPONTANEOUS REGRESSION OF SHOPE
PAPILLOMA VIRUS-INDUCED PAPILLOMAS OF
FETAL RAT SKIN TRANSPLANTED TO THE ADULT RAT.
(E.) Kreider, J. W. (Pennsylvania State U.,
Hershey) and C. Breedis. Fed. Proc. 28(2):686,
1969.

70-1328 HERPES-LIKE VIRUS ISOLATED FROM
LEUKEMIA SUSCEPTIBLE GUINEA PIGS. (E.)
Hsiung, G. D. (Yale U. Sch. Med., New Haven,
Conn.) and L. S. Kaplow. Fed. Proc. 28(2):697,
1969.

70-1329 CELL-MEDIATED COMPLEMENTATION OF DNA
VIRUSES. (E.) Jerkofsky, M. A.
(Baylor U. Coll. Med., Houston, Tex.) and F.
Rapp. Fed. Proc. 28(2):698, 1969.

See also abstract nos.: 1002,1009,1012,1025,1026,1032,1040,1202,1203

70-1330 MELANOMA IN TWINS. CUTANEOUS MALIGNANT MELANOMA IN IDENTICAL TWINS FROM A SET OF TRIPLETS. (E.) St-Arneault, G. (Roswell Park Mem. Inst., Buffalo, N. Y.), G. Nagel, D. Kirkpatrick, R. Kirkpatrick and J. F. Holland. Cancer 25(3):672-677, 1970.

Identical male twins, each with a pre-existing brown mole similarly located on the left chest, developed malignant melanomas at age 53 yr. The moles began to grow within 2 mo. of each other. A fraternal triplet (male) showed no evidence of any neoplasm. The mother died at age 78 from rectosigmoid cancer and 3 maternal aunts and 1 maternal uncle had histories suspicious of cancer.

70-1331 AN INCIDENT OF FAMILIAL CANCER INCLUDING 3 CASES OF OSTEOGENIC SARCOMA. (E.) Epstein, L. I. (Indiana U. Med. Ctr., Indianapolis), D. Bixler, and J. E. Bennett. Cancer 25(4):889-891, 1970.

A 40-yr.-old Caucasian male, whose right leg was removed when he was 15 because of an osteogenic sarcoma, was found to have a similar lesion of the maxilla. A study of his family over 3 generations showed that his father died at age 29 yr. of an adenocarcinoma of the colon, a sister had a squamous cell carcinoma removed from her forehead at age 20, and a brother died of spongioblastoma at age 6. The children of his sister and the 4 children of his mother after remarriage were free of cancer. Of the proband's 5 children, however, one died of an adrenal tumor at 13 mo., and another of an osteogenic sarcoma; 5 of his wife's pregnancies ended in spontaneous abortions.

70-1332 FAMILIAL MULTIPLE POLYPOSIS. A STATISTICAL STUDY OF A LARGE KENTUCKY KINDRED. (E.) Asman, H. B. (1169 Eastern Parkway, Louisville, Ky.) and E. R. Pierce. Cancer 25(4):972-981, 1970.

A survey of a kindred of 1,422 members (706 males, 667 females, and 49 unknown) over 7 generations revealed 72 medically-proven cases of familial multiple polyposis and 8 deduced cases. All the cases were among the descendants of 2 brothers, 53/935 from one and 27/411 from the other. A third brother and his descendants were free of the disease. The av. age at polyposis diagnosis was 27.7 yr. (ranging from 7-57 yr.), and cancer of the colon or rectum was diagnosed in 30 (41.7%) at an av. age of 38.8 yr. There was no significant sex difference in the incidence of carcinoma. Cancer was found within 2 yr. of polyposis diagnosis in 20/41 with prior symptoms and in 3/25 cases without prior symptoms. Also, the mean age of 21 cases with symptoms and cancer was 37.1 yr., while the mean

age for 20 cases with symptoms and without cancer was 25.4 yr.

70-1333 GENETIC RELATIONSHIPS IN FAMILIAL LEUKEMIA AND LYMPHOMA. (E.) Rigby, P. G. (Eugene C. Eppley Inst. Res. Cancer Allied Dis., Omaha, Nebr.), P. T. Pratt, R. C. Rosenlof and H. M. Lemon. Arch. Intern. Med. (Chicago) 121(1):67-70, 1968.

A survey in eastern Nebraska showed 39 families having more than one member with leukemia, 91/855 members in the affected families, with 77 sibling or parent-child pairs. There were 32 acute leukemias, 15 cases of Hodgkin's disease, 20 chronic lymphocytic leukemias, 6 lympho-sarcomas, 3 reticulum cell sarcomas, 3 giant follicular lymphomas, 5 myelomas, and 7 lymphomas. Similar diagnoses were seen in 28/77 pairs and including 20 families. The members of families with multiple cases died at earlier ages than single family cases.

70-1334 RHABDOMYOSARCOMA IN CHILDREN: EPIDEMIOLOGIC STUDY AND IDENTIFICATION OF A FAMILIAL CANCER SYNDROME. (E.) Li, F. P. and J. F. Fraumeni, Jr. (NCI, Bethesda, Md.). J. Nat. Cancer Inst. 43(6):1365-1373, 1969.

A survey of rhabdomyosarcoma was made between 1960 and 1964 which included 418 death certificates of U.S. children under 15 yr., and hospital charts of 280 children less than 16 yr. Of those who had died from this neoplasm during this time, 376 were white, 40 Negro and 2 were other nonwhites; the sex ratio was 6:5 for whites and 1:1 for nonwhites; and, the most commonly affected areas were the head, neck, urogenital organs and extremities. The peak mortality was at 3 yr. in both males and females, with no sex differences by site, except that 18/21 cases involving the upper extremities were males. Also, there was no significant space or seasonal clustering, and some time clustering only in the south Atlantic area. Breast cancer was seen in 6 mothers during or before the child's hospitalization and in 17/41 (41% as opposed to an expected 22%) of female relatives with a specific cancer. Soft tissue sarcomas were seen in the siblings of 3 cases (0.06 expected) and in 2 cousins. Neoplasms occurred in at least 1 grandparent of these 5 families and in a parent of all but one. Familial cancer syndrome involving multiple sites suggest that the component tumors share etiologic influences, and that these influences can be clarified by the best use of such occurrences for laboratory and epidemiologic research.

70-1335 MALFORMATIONS AND LEUKEMIA IN CHILDREN WITH DOWN'S SYNDROME. (E.) Fabia, J.

and M. Drolette. (Harvard Sch. Pub. Health, Boston, Mass.). Pediatrics 45(1, Pt. 1):60-70, 1970.

Malformations, other than those characteristic of mongolism, were seen in 863/2,421 (35.6%) cases of children with Down's syndrome born alive, between January 1, 1950 and January 1, 1967, to mothers residing in Massachusetts. There were 23 cases of leukemia (50 times the av. for children under 15 yr.), 5 of whom died before day 28 of life. In the early yr. of the survey, there was a high proportion of males, which reversed in the later yr., but the overall sex distribution was similar. The av. maternal age was 35.3 yr., with no correlation between maternal age and age of death of leukemia cases. Of 11 of these pts. karyotyped, 9 were trisomic and 2 were mosaics. Except for leukemia, there was no other case of malignancy associated with Down's syndrome pts. in this survey.

70-1336 THE CHRISTCHURCH CHROMOSOME (Gp⁻). MONGOLISM, ERYTHROLEUKEMIA AND AN INHERITED Gp⁻ CHROMOSOME (CHRISTCHURCH). (E.) Juberger, R. C. (U. Oregon Med. Sch., Portland) and B. Jones. New Eng. J. Med. 282(6):292-297, 1970.

The proband was an 18-mo.-old male with acute myeloblastic anemia and Down's syndrome. His only sibling, born about 10.5 yr. before, died 1 day after birth with multiple anomalies. The mother and the father were both healthy. The only member of either family with a hematologic disorder was a paternal uncle of the mother who died of leukemia at 61 yr. Chromosomal analysis of the proband showed 2 cell lines; 1 line had 47 chromosomes and 2 Gp⁻ chromosomes (deletion of short arms of a G group chromosome), the other had 51 chromosomes and 3 Gp⁻ chromosomes. The Gp⁻ chromosome was carried in the maternal line by the mother, grandmother and great-grandmother of the proband, all of whom were phenotypically normal. The mother was the only one of 3 daughters that received the Gp⁻ chromosome.

70-1337 SMOKING AND MORTALITY: A PROSPECTIVE STUDY. (E.) Weir, J. M. and J. E. Dunn, Jr. (Bureau Adult Health Chron. Dis., Berkeley, Calif.). Cancer 25(1):105-112, 1970.

A study relating cancer deaths and cigarette smoking was made on 68,153 men, 35-64 yr. old at time of entry, and who were observed for 5-8 yr. (av. 7.08), for a total of 482,658 person-years of observation. Data were collected in the period 1954-1957 from labor union members in specified occupations. Among the smokers (all men who were discontinued or continuing smokers of cigarettes), the risk of cancer of the mouth, larynx, esophagus, lung, kidney, and bladder were increased relative to the risk of non-smokers (including pipe and cigar smokers). The

risk of lymphomas, leukemia and cancer of the pancreas was also increased in smokers, but with inconsistencies probably due to the small numbers. The risk of lung cancer in smokers relative to nonsmokers increased with each decade up to age 55-64, then declined. Other diseases related to smoking, especially heart disease, are discussed. These findings are compared to other studies, and new directions for research are outlined.

70-1338 REPORT OF THE WORKING GROUP ON STUDIES OF CANCER AND RELATED DISEASES IN MIGRANT POPULATIONS. (E.) Haenszel, W. (Ed.) (U. Hawaii, Honolulu). Int. J. Cancer 4(3):364-371, 1969.

Migrant populations present an opportunity to investigate the influence of environment and host characteristics when studying the great variety of site-specific cancers throughout the world. Methods of study and a review of some continuing studies are presented, including g.i. cancer among Japanese migrants and cancer of the liver and nasopharynx among Chinese in Singapore; and the role of diet in carcinogenesis was discussed.

70-1339 A CLINICAL EXPERIMENTAL INVESTIGATION OF THE RATE OF CELL PROLIFERATION IN HUMAN MALIGNANT TUMOURS. (E.) Refsum, S. B. (U. Oslo State Hosp.) and P. Berdal. Acta Otolaryng. (Stockholm) 67(2-3):101-106, 1969.

Mitotic counts were made in malignant tumors after admin. of demecolcine (10 mg; i.v.), a mitotic inhibitor. The rate and range of cell proliferation/1000 cells/hour for various epithelia and tumors was as follows: mucous and serous glands, 0.5 (0.2-1.0); columnar and thin epidermoid epithelium (larynx/trachea), 4.8 (0.2-14.0); thick or hyperplastic epidermoid epithelium (mouth/tongue), 10.0 (3.0-25.0); atypical epithelium, 12.8 (0.8-33.0); and carcinomas, 11.48 (0.6-42.0). In all tissues there was a wide range in rate of cell proliferation, most pronounced in carcinomas and atypical epithelium where there was a 40-70-fold increase in rate from slow- to fast-proliferating regions. Many malignant tumors had a rate of cell proliferation equal to or less than normal epithelium, and rates varied in different areas within individual tumors. The considerable discrepancy between clinically measured growth and doubling time calculated on the basis of cell proliferation is due to cell loss, but how it occurs is unknown.

70-1340 THE APPLICATION OF A MATHEMATICAL MODEL DESCRIBING THE TIMES OF OCCURRENCE OF MESOTHELIOMAS IN RATS FOLLOWING INOCULATION WITH ASBESTOS. (E.) Berry, G. (Llandough Hosp., Penarth, Glamorgan, Wales) and J. C. Wagner. Brit. J. Cancer 23(3):582-586, 1969.

A mathematical model is presented relating the age-specific death rate of animals that died with mesotheliomas (m) to the time (t) after inj. of asbestos, where $m=0$ for t less than w , and $m=ck(t-w)^{k-1}$ for t greater than or equal to w ; c , k and w are constants relating to dose, the number of necessary changes to form a cancer cell, and latent period, resp. This model, corrected for the natural age-specific death rate, was applied to data for 8 groups of 84-96 rats. Of those inj. with asbestos, 30 to 70% developed mesotheliomas; the model gave a reasonable fit to all but one group. It is suggested that some animals in each group were resistant to asbestos-induced mesotheliomas.

70-1341 THE ROLES OF SYNTHESIS AND DEGRADATION IN THE REGULATION OF CATALASE LEVELS IN THE NEOPLASTIC TISSUES. (E.) Rechcigl, M., Jr. (NIH, Bethesda, Md.), Z. Hruban and H. P. Morris. *Enzym. Biol. Clin. (Basel)* 10(3): 161-180, 1969.

The catalase activity in hepatomas carried by several strains of rats (ACI/N, Sprague-Dawley, BUF/N, OM/N) ranged from moderate to high except for the rapidly-growing Novikoff, #3683 and #3924A hepatomas. Generally, no correlation was seen between enzyme level and growth rate. Kinetic studies were made by inj. rats with 3-amino-1,2,4-triazole (AT; 1 g/kg i.p.) and/or allylisopropylacetamide (AIA; 200 mg/kg i.p., 1-2 admin./day for the length of the experiment), but due to the appearance of AIA-resistant catalase in the hepatomas, the data were considered unreliable and only AT data were used. Hepatoma #5123 synthesized 0.92 U enzyme/hour compared to 3.88 U/hour in normal liver, and both degraded the enzyme 2.4%/hour. Similarly, in hepatoma #7316A, 2.30 U/hour catalase was formed compared to 4.00 U/hour in liver, and the rates of destruction were 2.6 and 1.9%/hour, resp.

70-1342 CANCER MORTALITY AND ENVIRONMENTAL TEMPERATURE IN THE UNITED STATES. (E.) Newell, G. R. (NCI, Bethesda, Md.) and D. E. Waggoner. *Lancet* 1(7650):766-768, 1970.

Age-adjusted death-rates from several types of cancer for white males and females during 1959-61 were correlated with measurements of temperature (mean annual temperature and range) for 9 census divisions of the U.S., including Alaska and Hawaii. Mortalities from many types of cancer were negatively correlated with temperature index, and positively correlated with both per-capita income and physician/population ratio. Among white males, the highest positive correlation (0.86) was for skin cancer, attributed more to sunlight exposure than temperature *per se*; for white females the positive correlation was 0.66. Cancer of the ovary had a high negative correlation (-0.95), while cervical cancer had a high

positive correlation (0.59); the latter is more common in lower socioeconomic groups. There was a high negative correlation for cancer of the esophagus for males (0-.80), but none among females. Deaths from cancer of the buccal cavity and pharynx correlated negatively with temperature index among males (-0.50) and positively among females (0.50). Males had a higher negative correlation for cancer of the bladder (-0.85) than did females (-0.59). Cancer of the liver and biliary tract had a negative correlation among females (-0.68), but none for males. It is suggested that geographical differences in cancer mortality may be associated with both artefacts and indirect causative factors, rather than reflecting a direct environmental effect on cancer risk.

70-1343 PHYSIOLOGICAL CHILLING AS A POSSIBLE FACTOR IN MORTALITY FROM NEOPLASIA. (E.) Krasnow, S. (Georator Corp., Manassas, Va.). *Int. J. Biometeor.* 13(1):87-92, 1969.

The wind chill index (physiologic still air equivalent temperature determined by the av. temperature and wind velocity) in January, 1959-1963, inclusive, was correlated in 50 U.S. counties (25 with the highest death rates and 25 with the lowest death rates from neoplasms of the digestive system, respiratory system and breast). In 163 large metropolitan areas, the temperature was as significant as the wind chill index. Death rates for neoplasms of the large intestine, rectum, stomach and breast were negatively correlated with temperature (co-efficient of correlation for digestive organs and breast were -0.939 and -0.490, resp., whereas death rates from malignancies of the respiratory tract were directly related (+0.711). Relationships for large intestine and rectal mortality were not linear, and had discontinuities at certain critical temperatures. Similar significant associations occurred for the number of days in the yr. in which frost occurred.

70-1344 DETECTION OF BREAST CANCER IN A SPECIALIZED CANCER DETECTION CENTER. (E.) Gilbertsen, V. A. (U. Minnesota Med. Ctr., Minneapolis). *Cancer* 24(6):1192-1195, 1969.

At the University of Minnesota Cancer Detection Center, 7,819 women (aged 45 and over) participated in the study for detection of breast cancer with a total of 40,633 examinations done between March 1, 1948 and February 28, 1969. Confirmed breast cancers were detected in 55 pts. During 1948-1964, breast cancer developed in 25 pts. in the interval between annual examinations. In the same time period, approx. two-thirds of the cancers (41) were detected at the center. From 1948 to February, 1964, 11/41 cancers were detected on first or initial examinations of 6,517 participants, giving a rate of 1.69 cancers/1,000 examinations. In subsequent

annual examinations that totalled 20,897, 30 additional cancers of the breast were discovered, for 1.44 cancers/1,000 subsequent examinations. The overall survival rate at 5 yr. was 86% and the age adjusted rate was 94%. The combination of yearly examinations by a physician and interim self-examination resulted in early detection of breast cancer which, when detected prior to recognized lymph node spread, has much improved 5- and 10-yr. survival rates over the general population.

70-1345 LACK OF TIME-SPACE CLUSTERING OF CHILDHOOD LEUKEMIA IN LOS ANGELES COUNTY, 1960-1964. (E.) Glass, A. G. (NCI, Bethesda, Md.) and N. Mantel. Cancer Res. 29(11):1995-2001, 1969.

Age, sex, date of death and residence were obtained from the death certificates of 298 white children under 15 yr. of age, who died of leukemia in Los Angeles County from 1960-1964. The data was analyzed using the Knox approach (2 cases are related if they are within a specified spatial and temporal distance of each other) and the Mantel approach (relating the reciprocal of the spatial separation to that of the temporal separation). No indication of space-time clustering, was found by either method, whether applied to age groups 0-5, 2-9 or 0-14 yr.

70-1346 BREAST TUMOURS IN INFANTS AND CHILDREN: A 40-YEAR REVIEW OF CASES AT A CHILDREN'S HOSPITAL. (E.) Simpson, J. S. (Hosp. Sick Child., Toronto, Ontario, Canada) and A. J. Larson. Canad. Med. Ass. J. 101(2):100-102, 1969.

7-mo.-old male North American Indian was admitted to the hospital because of a rapidly-growing mass about 5 cm in diameter in one breast. Histologic examination revealed an intraductal papilloma similar to such a tumor occurring in an adult. This is believed to be the youngest patient with this type of tumor reported in the literature. Breast tumors in 8 other children were described (5 fibroadenomas, 2 hemangiomas of the areola and 1 carcinoma, juvenile-type). None showed discharge or regional lymph node enlargement. All lesions were treated by local excision; no recurrences have been recorded.

70-1347 CLINICAL STUDIES OF TUMORS IN CHILDREN UNDER 15 YEARS OF AGE, WITH SPECIAL REFERENCE TO NEUROBLASTOMAS. (E.) Tsunooka, H. (Nagoya City U. Med. Sch., Japan). Nagoya Med. J. 14(4):221-250, 1968.

survey of the records of all pts. under 15 admitted to the second Department of Surgery, Nagoya City University Medical School Hospital from April 1, 1949 - October 30, 1968 yielded

119 verified neoplasms (111 in pts. and 8 in referrals). Tumors of neural origin were the most common (34), followed by angiomas (29), teratomas (14), and embryonal tumors of the viscera (9); there were only 8 tumors of epithelial origin. Malignant tumors comprised 52.1% of the total (38/49 embryonal tumors, 52/77 deep tumors, 34/55 abdominal and 27/31 retroperitoneal neoplasms), and were observed in 39 males as opposed to 23 females; 27 males and 30 females had benign tumors. The most common site for all tumors was the abdomen (55) and about 66% of all neoplasms were located deeply. The 14 neuroblastomas are discussed in detail.

70-1348 TUMORS OF INFANCY AND CHILDHOOD. (Ger.) Erdős, Z. (Univ. Ist. Pediat. Clin., Budapest), L. Szöke, M. Szeder and A. Török. M Schr. Kinderheilk. 117(5):415-418, 1969.

An examination of the records of the pediatric division of the University Hospital in Budapest, from 1947-1966, inclusive, showed that the proportion of malignant tumors/1000 admissions under 14 yr. has not increased significantly over the past 20 yr., despite reports in both Hungarian and foreign journals of a marked increase of malignancy of childhood. However, among the population of Hungary as a whole, a slow but significant increase of tumor mortalities has been in evidence over about the same period of time (from 12.40/10,000 population in 1948 to 19.14 in 1965), and a similar trend appears to be seen with respect to childhood leukemias and cerebral tumors in children.

70-1349 MULTIPLE MYELOMA IN OLMSTED COUNTY, MINNESOTA, 1945-1964. (E.) Kyle, R. A. (Mayo Clin., Rochester, Minn.) F. T. Nobrega and L. T. Kurland. Blood 33(5):739-745, 1969.

All cases of multiple myeloma diagnosed in residents of Olmsted County, Minnesota, during the 20-yr.-period 1945-1964 were identified and reviewed. There were 35 cases of multiple myeloma, 22 men and 13 women. The av. annual incidence rate for the total population was 3.1/100,000 in each decade (1945-1954, and 1955-1964). When age-adjusted to the 1950 United States white population, the rates were virtually identical to the crude rate, 2.9 and 3.0/100,000, resp. The overall incidence rate for the 20-yr.-period for males was 4.1/100,000, while that for females was 2.2/100,000, a ratio of 1.9:1. When computed for persons 30 yr. of age and over, the av. annual incidence rate was 6.3/100,000. There was no significant difference in urban-rural rates. Age-specific rates increased with age.

70-1350 CARCINOMA OF THE GALLBLADDER. (Pol.) Karwowski, A. (Acad. Med. 2nd Surg.

Clin., Warsaw), B. Rybaczek, E. Synowiedzka, E. Ruszkowska, A. Korzeniowska and M. Krawczyk. Pol. Tyg. Lek. 24(21):799-801, 1969.

A survey of 10,402 autopsies performed between 1945-1967 revealed 306 cases (248 women, 58 men) of gallbladder cancer (2.94%) and gallbladder stones in 1,904 (18.3%). Bile calculi were present in 193/306 cancer cases (63.06%). The majority (85%) of these cancer pts. were 50-80 yr. old, only 4 were under 40 yr. Analysis of 1,141 cholecystectomies performed between 1957-1967 revealed 76 cases (72 women, 4 men) of gallbladder carcinoma (6.66%). In 39/76 bile calculi were also found, and 52/76 (68.5%) had a long history of symptoms indicating that bile calculi frequently precede gallbladder cancer and that neoplastic change in the gallbladder is more frequent than generally assumed.

70-1351 CANCER OF THE LUNG IN UTAH. A COOPERATIVE STUDY BY THE UTAH THORACIC SOCIETY AND THE INTERMOUNTAIN REGIONAL MEDICAL PROGRAM TUMOR REGISTRY. (E.) Jenson, C. B. and C. R. Smart. Rocky Mountain Med. J. 66(1):47-50, 1969.

A review of 1,018 cases of lung cancer in the Utah State Tumor Registry recorded between January, 1957 and November, 1968 showed 889 males and 129 females. Pulmonary neoplasm was only the sixth most frequent cancer in Utah, being preceded by neoplasms of the breast, skin, colon and rectum, cervix and prostate. Between 1940 and 1950, the U.S. rate of lung cancer rose by 96%, but in Utah it only rose by 17%. From 1950-1960, the increase in the entire U.S. was 57%, while the Utah increase was 34%. In the last 5 yr. recorded, Utah surpassed the national rate with a 37% increase, compared to the national increase of 21%. The cause of this increase was not apparent. One of the factors responsible for lower general incidence in Utah may have been below-average tobacco consumption per person, which was less than half the U.S. average. Lag intervals between symptoms, diagnosis and treatment, stage of disease, treatment and survival are presented.

70-1352 CANCER OF THE CERVIX IN UTAH - AN ANALYSIS OF 1084 CASES. (E.) Herbertson, R. M. (U. Utah, Salt Lake City) and C. R. Smart. Rocky Mountain Med. J. 66(6):39-42, 1969.

A total of 1,084 cases of cervical carcinoma were reported in Utah between January, 1956 and December, 1968. There were 155, 136 and 137 new cases reported during 1965, 1966 and 1967, resp., for an incidence of 28/100,000 females. The av. age of those having in situ lesions was 39.6 yr., and of those with invasive lesions, 49.7 yr. Of the total group, 599 (55%) were non-invasive. Of in situ tumors, 84% occurred before age 50,

with peak incidence between the third and fourth decades of life. The overall 5-yr. survival rate for those with invasive lesions was 70%, and for those with in situ lesions, 96.7%. Of those with localized lesions, there was a 5-yr. survival rate of 78.6%.

70-1353 GEOGRAPHIC AND SECULAR VARIATIONS IN MALIGNANT DISEASE IN OKLAHOMA, 1956-1965. (E.) Assal, N. R. (U. Oklahoma Sch. Health, Oklahoma City) and R. D. Lindeman. J. Okla. Med. Ass. 62(10):473-482, 1969.

Mortality data for carcinoma of the breast, cervix uteri, corpus uteri and uterus, ovary and prostate gland in Oklahoma were assessed for the two 5-yr. periods (1956-60 and 1961-65) to establish secular trends, by sex, race and age. Among non-white and white females, carcinoma of the cervix was the number 1 and 4 cause of death, resp., while that of breast ranked 2 and 1, resp., and ovary, 8 and 5. Prostate carcinoma ranked 1 and 2, resp., as the most common site of carcinoma in non-white and white males. Secular trends for the 2 five-yr. periods showed a decline in death rates for carcinoma of the cervix uteri, corpus uteri and uterus, and stable death rates from carcinoma of the breast, ovary and prostate. Non-whites had much higher mortality rates from carcinoma of the cervix uteri, corpus uteri, uterus and other female organs and carcinoma of the prostate. Carcinoma of the cervix was highest among eastern counties of the state, an area of low socioeconomic status. Breast carcinoma mortality increased significantly with degree of urbanization. Carcinoma of the prostate was more prevalent in the northwestern upper socioeconomic counties of the state. The various geographic, racial and secular trends are discussed.

70-1354 MULTIPLE PRIMARY MALIGNANT NEOPLASMS. (E.) Campbell, L. V., Jr. and A. L. Watne (West Virginia U. Med. Ctr., Morgantown). Arch. Surg. (Chicago) 99(3):401-405, 1969.

A survey in the Tumor Registry of the West Virginia University Medical Center between August, 1960 and July, 1967 showed 165/2,594 (6.4%) pts. with multiple primary malignant neoplasms (103 males, 62 females). The av. age at diagnosis of the first neoplasm was 60.9 yr. (range, 24-99 yr.). In those diagnosed as having a single malignant neoplasm, 4% developed a second; in those diagnosed with 2 malignancies, 8.7% developed a third. A greater-than-expected incidence (20%) of cancer of the oral cavity and larynx was found in pts. with an initial pulmonary neoplasm. Hormonal influence in multiple malignancies of female genitalia is also discussed.

70-1355 INCIDENCE OF CUTANEOUS CANCER IN MINNESOTA. (E.) Lynch, F. W. (U.

Minnesota Med. Sch., Minneapolis), H. Seidman and E. C. Hammond. Cancer 25(1):83-91, 1970.

survey was made in Minnesota of 2,596 cutaneous cancers (excluding lymphomas, reticulosis and leukemia and cancer of the anus, penis, vulva and free margin of the lip) in 2,358 pts. first diagnosed in 1963 by radiologists, pathologists and dermatologists. The observed number of cases was high in relation to expectation based on various tumor registries and on differing assumptions. The incidence rates were 71.5/100,000 in and 47.2/100,000 women, and rose with age in both sexes. For all sites and for cancer of the face, neck and head, the male:female sex ratio was 1.5:1. Basal cell carcinoma of the lower extremities was 3 times more common in women, with no squamous cell carcinoma of the lower extremities in men. The incidence rate of melanoma was twice as high in females. Rates of squamous cell carcinoma were three times higher in men, mostly attributed to carcinomas of the lip and ear.

1356 LACTATION AND REPRODUCTIVE HISTORIES OF BREAST CANCER PATIENTS IN BOSTON, 1965-66. (E.) Salber, E. J. (Harvard Sch. Public Health, Boston, Mass.), D. Trichopoulos and B. MacMahon. J. Nat. Cancer Inst. 43(5):1013-1024, 1969.

survey from January 1, 1965-December 31, 1966 revealed all new cases of breast carcinoma diagnosed in white female residents of Boston and vicinity revealed 758 cases, with an av. annual rate of 15.5/100,000 female population. Of these, 606 were interviewed, together with 1,807 pts. with diseases other than breast cancer. After exclusion of interviews considered to be unreliable, 580 cases were compared to 1,737 controls. There were 40% more single women with breast cancer (15/100,000) than married women (82/100,000). The number of foreign-born women (125) was less than the expected number of 145.8; there were more Jews than expected (122 as opposed to 94.4) and less Protestants (123 as opposed to 148.4); and no clear trend was observed with socioeconomic status. Breast cancer risk increased with increasing parity, except in the sixth and seventh decades, and there was no significant difference between cancer incidence in married and single nulliparous women. The risk of cancer for women having a first pregnancy at or 30 yr. was 2.1 times that of women with a first pregnancy before she reached 20 yr. The parity relationship between breast cancer and lactation indicated an increased risk. No correlation with menstrual history was seen.

1357 A CONTROLLED STUDY OF THE CONSTITUTIONAL STIGMATA OF ENDOMETRIAL ADENOCARCINOMA. (E.) Fox, H. (U. Manchester, England) and D. K. S. Brit. J. Cancer 24(1):30-36, 1970.

A survey of 300 consecutive cases of adenocarcinoma of the endometrium was contrasted to a control group of 300 women drawn from surgical and medical wards, screening out those suffering from malignant disease or a condition specifically associated with obesity, hypertension, diabetes mellitus or endocrine disorder. A significant difference was observed between the adenocarcinoma group and the controls when comparing the mean age at menopause (49.1 and 47.9, resp.), marital status (58 single compared to 35), and nulliparity (112 compared to 71). There was no significant difference when comparing the number of women with hypertension (106 and 75, resp.), obesity (102 compared to 94), diabetes mellitus (11 and 9), thyroid disease (13 compared to 18) and extragenital malignant disease (both 6).

70-1358 PRIMARY CARCINOMA OF FALLOPIAN TUBE. (E.) Cohn, S. (Long Island Jewish Hosp., New Hyde Park, N. Y.), R. W. Rossano and A. N. Fenton. New York J. Med. 69(10):1321-1328, 1969.

From April, 1962-January, 1967, 4 women with primary Fallopian tube tumors were admitted to 2 neighboring hospitals. These 4 pts. comprised about 1:5500 gynecological admissions and about 0.38% of all female genital cancers seen during this period. The possible precipitating role of salpingitis is discussed. In 3/4 pts., who showed unilateral tumors associated with chronic bilateral salpingitis of many yr. duration, the tumors did not seem to spread beyond the tube. In the fourth pt. with no signs of salpingitis, invasion of the pelvic wall through the later tubal end was noted.

70-1359 INCIDENCE OF MULTIPLE PRIMARY CANCERS. II. INDEX CANCERS ARISING IN THE STOMACH AND LOWER DIGESTIVE SYSTEM. (E.) Schottenfeld, D. (Mem. Hosp. Cancer Allied Dis., New York, N. Y.), J. W. Berg and B. Vitsky. J. Nat. Cancer Inst. 43(1):77-86, 1969.

During 1949-1962, 6,627 pts. with cancer of the stomach and lower digestive tract were screened for occurrence of other primary cancers. In pts. with stomach cancer, development of a subsequent cancer of the reproductive organs, kidney and the urinary bladder occurred less often than expected. There was no increase of simultaneous tumors of other organs in pts. with cancer of the stomach or digestive organs proximal to the colon and rectum. Of pts. with cancer of the colon or rectum, 1.9% had a prior history of large intestinal cancer, and 3.6% had simultaneous multiple primary cancers of the large intestine; the observed/expected (O/E) ratio of the number with subsequent multiple primary neoplasms of the large intestine was 3.1 and for multiple primary neoplasms at other sites, 1.2. The cecum had the highest O/E ratios, 6.3 and 2.4, resp.

70-1360 BILIARY TRACT CARCINOMAS. (Ger.)
Nordeck, E. (Evangel. Hosp., Göttingen-Weende, Germany) and P. E. Böhme. Langenbecks Arch. Klin. Chir. 323(4):279-291, 1969.

Analysis of 1,418 biliary tract operations performed between 1952-1967 at the Göttingen-Weende Hospital revealed 45 (3.2%) confirmed carcinomas of the biliary tract, including 20 gallbladder (1.4%), 7 porta hepatica (0.5%), 5 choledochus (0.4%), 13 duodenal papilla (0.9%) and 35 unconfirmed carcinomas. No increase in frequency of gallbladder carcinoma was seen, but frequency of confirmed papillary carcinoma increased from 0.37% in 1952-1955 to 1.8% in 1964-1967, and of unconfirmed from 1.75% to 1.3%, resp. No biliary tract carcinomas were found among pts. less than 40 yr. old, the greatest number occurred in those 60-69 yr. old. While gallbladder carcinomas were found exclusively in women, 38% of papillary carcinomas were detected in men. Histologically, the most frequent was adenocarcinoma, followed by solid carcinoma. Metastases in the liver were present in gallbladder (15%), porta hepatica (14%), duodenal papilla (18%) and none in choledochal carcinoma. The duration of symptoms usually was longer in those with gallbladder (7-12 mo.) than those with other biliary tract carcinoma (2-6 mo.). It is suggested that since the increase in biliary tract carcinoma in this study was due almost exclusively to an increase in duodenal papilla carcinoma (frequently difficult to differentiate from carcinoma of the head of the pancreas), conclusions as to an increase in biliary tract carcinoma in recent yr. should be reached with extreme caution. A clear differentiation of location of the carcinoma in the biliary tract is recommended.

70-1361 MICROINVASIVE CARCINOMA OF THE UTERINE CERVIX. (E.) Ng, A. B. P. (Case Western Reserve U. Inst. Path., Cleveland, Ohio) and J. W. Reagan. Amer. J. Clin. Path. 52(5): 511-529, 1969.

Among 781 squamous cell carcinomas of the cervix at the Institute of Pathology of the University Hospitals of Cleveland and Case Western Reserve University between 1943 and 1967 inclusive, 66 microinvasive carcinomas were seen. Dividing the 25 yr. into 5-yr.-periods, the number of squamous cell carcinomas decreased from 242 (1943-1947) to 115 (1963-1967), while the microinvasive cases increased steadily from 3 to 24. The mean age of the 66 pts. when the carcinoma was detected was 46.9 ± 12.7 , ranging from 24-74 yr. Clinically, 25 were asymptomatic with normal cervical findings, 16 were asymptomatic with abnormal cervical findings, 12 had symptoms but a normal-appearing cervix, and 13 had both symptoms and abnormal findings. The av. linear extension of the lesion was 3.30 ± 1.5 mm, and none penetrated beyond a depth of 5 mm.

70-1362 RHABDOMYOSARCOMA IN CHILDREN. (Sp.)
Salas-Martínez, M. (Child. Hosp., Mexico) and O. Angulo-Hernández. Gac. Med. Mex. 99(4):405-416, 1969.

Between 1943-1968, inclusive, the Children's Hospital of Mexico recorded 94 cases of tumor of the soft tissue in children 11 yr. old and under, including rhabdomyosarcoma (27/94), fibrosarcoma (19/94), undifferentiated sarcoma (18/94), liposarcoma (10/94), angiosarcoma (6/94), malignant mesothelioma (4/94), leiomyosarcoma (3/94), 2 cases, each, of malignant mesenchymoma and myoblastoma, and 1 case, each, of myxosarcoma, malignant synovium, and malignant hemangiopericytoma. The primary sites of the rhabdomyosarcomas were the head and neck (13/27), trunk (3/27), gluteal region (3/27), thigh (3/27), leg (2/27), and 1 case, each, in the anterior abdominal wall, mediastinum, and retroperitoneal region. A total of 22/27 were composed of embryonal tissue, 4/27 of alveolar tissue, and 1/27 was pleomorphic. Two of 27 were first recurrences; 1/27, each, was a second and third recurrence. Metastasis to regional lymph nodes had occurred in 16/27, metastasis to the lungs in 8/27, endocranial extension in 3/27 and intrapelvic extension in 1/27. Age at onset was as follows: less than 1 yr. = 1/27, 1-3 yr. = 12/27, 3-5 yr. = 5/27, 5-7 yr. = 6/27, 7-9 yr. = none, 9-11 yr. = 3/27. The male:female ratio was 16:11.

70-1363 THE AETIOLOGY OF CARCINOMA OF THE UTERINE CERVIX IN SOUTH INDIA: A PRELIMINARY REPORT. (E.) Shanta, V. (Cancer Inst., Madras, India) and S. Krishnamurthi. Brit. J. Cancer 23(4):693-701, 1969.

A total of 473 South Indian women in-patients at the Cancer Institute of Madras with squamous cell carcinoma of the cervix were interviewed and examined, along with 553 controls, between 1958-1961. There was no significant difference in the marital histories of the 2 groups, including age and number of marriages, parity and instrumental deliveries. No cases of cervical cancer were observed in Catholic nuns and there was a much lower percentage of nulliparous women among the cases. Few of the women, cases or controls, had extra-marital relations, while many of the men did. Only 0.8% of the cases were Moslem compared to 9.9% in the population, probably due to the Moslem practice of circumcision in the male. There was no significant correlation with syphilis, leukorrhea, diabetes mellitus, anemia, avitaminosis, tuberculosis, hormonal status, regional distribution, diet, occupation, blood group, douching and use of contraceptives.

70-1364 SKIN CANCER IN SAURASHTRA. (E.)
Godbole, V. K. (M. P. Shah Med. Coll.,

Amnagar, India), H. T. Toprani and H. H. Shah. Indian J. Path. Bact. 11(3):183-189, 1968.

of 133 cases of skin cancer reported for the 5-yr.-period January, 1960-May, 1967 from the Gujarat region of Gujarat, India and classified according to the World Health Organization scheme, 126 were primary skin cancer and 7 were metastatic carcinoma of the skin. Of the 126 cases of primary skin cancer, 105 (83.2%) were squamous cell carcinoma, 14 (11.2%) were basal cell carcinoma, 2 (1.6%) each were sweat gland carcinoma and melanocarcinoma, and 1 (0.8%) each were adenoacanthoma, sebaceous epithelioma and melanoplastic carcinoma. Mean age of persons with squamous cell carcinoma was 41.1 yr., and basal cell carcinoma, 56.7 yr. Six of 102 cases (5.7%) of squamous cell carcinoma were in the age group 0-14 yrs. All cases of basal cell carcinoma were localized to the face and scalp; 5 were of the reticulated type, 5 were adenocystic and 6 were basosquamous. Most cases of squamous cell carcinoma were in the trunk (24.8%), lower limbs (22.9%) and face.

70-1365 AGE DISTRIBUTION AND LOCALIZATION OF SKIN CANCERS. (Ger.) Krause, W. (U. Giessen Derm. Clin., Germany) and C. Soll. Z. Haut. Geschlechtskr. 44(17):575-580, 1969.

Analysis of 2036 pts. (1165 men, 871 women) with middle cell carcinoma treated between 1954-1968 in the clinic in Giessen, Germany revealed a morbidity increase with age (adjusted) and highest morbidity in tenth decade of life. In 80% of men and 76% of women carcinomas were localized to the face. Among men they occurred most frequently on the lower lip, nose and ear, and among women on the forehead, nose, cheeks and lower lip. Differences in "carcinoma density" (number/cm²) were noted; it was greater on the nose among men and on forehead among women. These differences were attributed to different exposure to sunlight (the ears being covered by hair in women, forehead by hats or caps in men). The high incidence and great carcinoma density on the lower lip was attributed to smoking rather than sunlight, which was also substantiated by a greater frequency among younger pts.

70-1366 INCIDENCE OF TROPHOBLASTIC NEOPLASIA IN IRAQ. (E.) Ghali, F. H. (Med. Coll., Baghdad, Iraq). Amer. J. Obstet. Gynec. 135(6):992-993, 1969.

Records of hydatidiform mole and choriocarcinoma from the Republican Hospital and Central Pathology Institute in Baghdad for the 5-yr.-period, 1960-1964, were reviewed. During that time, there were 100 pts. with hydatidiform mole and the total number of pregnancies was 22,147, giving an occurrence rate of 1:221 pregnancies. The occurrence of hydatidiform mole in relation to the total number of deliveries was 1:276. Among

156 gynecological cancer pts. admitted to the hospital, there were 28 cases of choriocarcinoma (17.9%). A similarly high incidence of choriocarcinoma was found in biopsy material at the Central Pathology Institute; among 418 gynecological cancer specimens, 93 (22%) were choriocarcinoma. It is concluded that the incidence of these 2 entities is much higher in Iraq than in Europe and the U.S.

70-1367 THE INCIDENCE OF NEOPLASTIC TROPHOBLASTIC DISEASE IN AUSTRALIA. (E.) Steigrad, S. J. (St. John's Hosp., Essex, England). Aust. New Zeal. J. Obstet. Gynec. 9(2):100-102, 1969.

The incidence of hydatidiform mole and choriocarcinoma over a 16-yr.-period (1950-1966) was analyzed for 3 major hospitals in Sydney. There were 251 hydatidiform moles and 19 choriocarcinomas. For hydatidiform mole the incidence rate was 1/962 confinements, and 1/1,103 pregnancies. For choriocarcinoma, the incidence was 1/12,705 confinements and 1/14,567 pregnancies. In Australia the incidence of trophoblastic disease is more than twice that in any other Caucasian country, but none of the proposed etiologic factors suggested by Acosta-Sison (1959), such as diet, ethnic race or poor social conditions, prevail. This tends to cast doubt on the traditionally accepted factors for trophoblastic disease.

70-1368 THE EXCRETION OF 3-HYDROXYANTHRANILIC ACID AND QUINOLINIC ACID IN UGANDA AFRICANS. (E.) Crawford, M. A. (Zool. Soc. London Nuffield Inst. Compar. Med.), I. L. Hansen and A. Lopez. Brit. J. Cancer 23(3):644-654, 1969.

A high urinary conc. of 3-hydroxyanthranilic acid (14-17 µg/ml) was found in healthy young adult Ugandans living in the north Lake Victoria shore region where the staple diet consists of plantains, root crops and soft fruits, as compared to urinary levels (2.3-5.5 µg/ml) of people living in the northern regions consuming milk and cereals. The av. 24-hr. excretion was 16 mg as opposed to 1.1 mg. Kynurenine and quinolinic acid, other metabolites in the same pathway, were also significantly higher in plantain eaters, but little difference was observed in levels of N-methyl nicotinamide. Levels of kynurenine acid and xanthurenine acid were raised, but not enough to indicate a vitamin B₆ deficiency. Changing the diet of one person from plantain to rice, meat, milk and European potatoes lowered his 3-hydroxyanthranilic and kynurenine excretion to levels comparable to those of Europeans.

70-1369 THE INCIDENCE OF CANCER OF THE OESOPHAGUS IN WEST KENYA. (E.) Ahmed, N. and P. Cook (M. R. C. Statistical Res. Unit,

London). *Brit. J. Cancer* 23(2):302-312, 1969.

From 1963-1965, esophageal cancer comprised 30% of the cancers seen in the Kisumu Government Hospital in western Kenya, while it was relatively rare 80 miles to the southwest and 150 miles to the west. Part of the reason for this higher incidence is the selective referral of esophageal cancer pts. to this hospital. There were 8 times as many cases of esophageal cancer in 30-60-yr.-old males, as would be expected from the incidence in Kyadondo County, Uganda and twice as many as in Johannesburg. The incidence of all other cancers in pts. of the same age group was 0.5 and 0.25 of that from these areas, resp. Adjusting for under-reporting, the age-standardized incidence of esophageal cancer would be 106-169/100,000 instead of the 37.1/100,000 observed. The observed male/female ratio was 10.6:1.

70-1370 EPIDEMIOLOGY OF PLEURAL MESOTHELIOMAS. A CURRENT REPORT OF 119 CASES IN THE HAMBURG AREA. (Ger.) Dalquen, P. (Harburg Gen. Hosp., Hamburg, Germany), A. F. Dabbert and I. Hinz. *Prax. Pneumol.* 23(8):547-558, 1969.

A total of 119 cases of pleural mesothelioma were seen in 3 hospitals and a tuberculosis sanitarium in Hamburg during the years 1958-1968, inclusive. Included were 79 men, 40 women, all over 30 yr. of age. The diagnosis was confirmed at surgery or autopsy in 44/119, by biopsy in 40/119, by clinical and X-ray findings alone in 35/119. Investigation showed that 51/119 lived or had lived in close proximity to an asbestos factory in the city, while occupational or other direct exposure to asbestos was definitely established in 17/119 and highly probable in 34/119. The mean period of known exposure was 12.2 yr. (range = 14 days to 41 yr.). The mean period between exposure and diagnosis of tumor was 35.2 yr. (range = 11-48 yr.). Among 93/119 who had died by the time of report, survival times after diagnosis had ranged from 3 mo. to 8 yr. (mean = 1 yr.).

70-1371 KAPOSI'S SARCOMA IN IBADAN. (E.) Oluwasanmi, J. O. (U. Ibadan, Nigeria) and B. O. Osunkoya. *W. Afr. Med. J.* 18(3):89-94, 1969.

Files of the Cancer Registry of the University College Hospital, Ibadan for April, 1960-April, 1968 were reviewed for Kaposi's sarcoma. There were 29 cases, all males age 12-69 (mean 41) yr., of various occupations and coming mostly from the western (10 cases/10 million population) and midwestern (7 cases/2.5 million population) regions of Nigeria. The initial lesion was on the feet or ankles (6 cases), calf and legs (4), thigh (1) and upper limbs (3); the most common symptom was the presence of a

nodule(s) and, next, pain. The characteristics of the disease were similar to those seen elsewhere.

70-1372 DISEASES AND DISEASE COMPLEXES AFTER AGE 60 ACCORDING TO AUTOPSY FINDINGS. (Ger.) Theuring, F. (Magdeburg Med. Acad. Inst. Path., Germany). *Z. Alternforsch.* 21(3):213-232, 1968.

Analysis of incidence of primary, secondary and associated diseases among autopsy material from 2,500 persons over age 60 revealed malignant tumors as primary disease in 801 (32%) (461 male, 340 female). Leukemias decreased with age (from 2.4% at 70 to 0% at 90 for both sexes). Frequency of malignant tumors decreased from 40.1% at age 65-69 to 17.9% at 90 (both sexes), whereas the frequency among men was higher (43.9% and 25.9% resp.) than among women (35.4% and 12.5%, resp.). Among women the most frequent (in descending order) were carcinomas of the uterus, stomach, intestines, breast and gallbladder, whereas uterus carcinomas decreased with advancing age and those of stomach and intestine increased. Among males, most frequent were carcinomas of the lungs, g.i. tract, prostate, bladder and skin. As a secondary disease, gallbladder carcinoma occurred after cholelithiasis (primary) in 14, cancerized ovarian cystoma after ovarian cystoma in 7, primary liver carcinoma after liver cirrhosis in 6, gastric carcinoma after gastric ulcer in 5, liver carcinoma after Thorotrast inj. in 2, and lung carcinoma (2) after tubercular lesions of the lung in 2.

70-1373 INCIDENCE OF MALIGNANT NEOPLASMS OF THE STOMACH IN POLAND AND THE CITY OF WARSAW - MORTALITY FROM NEOPLASMS IN POLAND IN THE YEARS 1962-1964. (E.) Gadomska, H. (Inst. Oncol., Warsaw), T. Koszarowski and Z. Drożdżewska. *Acta Med. Pol.* 9(4):359-363, 1968.

Among men in Poland in 1964, cancer of the stomach was the most frequently reported malignant neoplasm, accounting for 24.1% of all neoplasms, while among women it accounted for 11.5%, ranking third after cancer of the uterine cervix (24.4%) and breast (12.6%). During the period 1962-1964, the percentage of registered new cases and deaths from cancer of the stomach in men greatly exceeded that in women, with a male:female sex ratio of 1.9. In the city of Warsaw in 1964, the incidence of stomach cancer among men was 42.2/100,000, second only to cancer of the bronchus and lung (48.2/100,000); incidence of stomach cancer among women was 28.1/100,000, ranking third after that of the cervix uteri (53.9) and breast (39.8). In 1964 the incidence rate among men for urban and rural areas were nearly identical, 24.8. For women in 1964, it was higher for urban (14.1/100,000) than for rural (12.1/100,000) areas. When related to age distribution, incidence rate of malignant tumors

gan to increase for males at age 45-49 yr. (174.7) and reached a max. at 65-69 yr. (174.7). Since 1960, deaths from cancer of the stomach were much more frequent in rural than in urban areas.

1374 PRIMARY HEPATOMA IN UGANDA. A PROSPECTIVE CLINICAL AND EPIDEMIOLOGIC STUDY OF FORTY-SIX PATIENTS. (E.) Alpert, M. E. Massachusetts Gen. Hosp., (Boston), M. S. R. and C. S. Davidson. Amer. J. Med. 46(5): 480-482, 1969.

Primary hepatomas in 46 pts. were studied in Kigo Hospital, Uganda over a 9-mo.-period from September, 1966-May, 1967; this represented 1% of all medical admissions. The age peak was 45 yrs. and the male:female ratio was 2:1. The disease was more frequent among poorer migrants from Rwanda-Burundi (12 cases or 3.6% of medical admissions) than in the local Baganda (22 cases or 2.1% of medical admissions). Interviews revealed no significant differences in medical, nutritional or alcoholic history between the pts. studied (421), neighbor controls (1) or hospital controls (38). About half of the pts. with hepatoma and their neighbors admitted to frequent (daily or more) beer ingestion and a third of the pts. to frequent ingestion of spirits. Native beers were brewed from various grains and contained 6-10% alcohol by volume. Several features of primary hepatoma in Uganda and the United States are compared. Possible etiologic factors in the high incidence of hepatomas in the Rwanda and Burundi tribes are discussed.

1375 GASTRIC CANCER INCIDENCE IN THE CRACOW REGION. (E.) Kołodziejaska, H. (Inst. Oncol., Cracow, Poland) and H. Nosek. Acta Med. 9(4):365-367, 1968.

The incidence rate of gastric cancer in the Cracow region of Poland in 1962-63 and 1966 was 27.5/100,000. In 1966, the incidence was 27.5/100,000 population, 36/100,000 for men and 16/100,000 for women. The incidence was higher in rural than in urban areas; this rural-urban gradient was more marked for men than for women. Among men, the incidence rates per 100,000 for Cracow city, small towns and rural areas were 20.5, 36.8 and 41.0, resp.; among women, these values were 18.8, 21.7 and 19.2, resp. The highest rates for both sexes were recorded between 60-69 yr.

1376 STATISTICAL ANALYSIS CONCERNING THE OCCURRENCE OF MALIGNANT TUMOURS IN THE DISTRICT OF ČESKÉ BUDĚJOVICE DURING THE PERIOD 1957-1966. (E.) Ondok, J. (Czechoslovak Acad. Sci. Inst. Botany, Prahonice) and V. Svoboda. Neoplasma (Bratisl.) 16(1):89-99, 1969.

A statistical analysis of cancer incidence in 1957-1966 was made for 119 localities in the district of České Budějovice (population in 1963 of 143,920) for the purpose of correlating significant fluctuations with specific characteristics of the environment. During the 10-yr.-period, 4,108 malignant tumors were recorded according to type, but there was no significant difference in tumor incidence within the district, including geographically different areas with different degrees of atmospheric radioactivity.

70-1377 ACUTE LEUKEMIA IN CHILDREN IN THE PROVINCE OF SASKATCHEWAN, 1961-66. (E.) Klaassen, D. J. (Ontario Cancer Found. Ottawa Civic Hosp., Canada). Canad. Med. Ass. J. 101(7):87-90, 1969.

All cases of acute leukemia in children aged 14 yr. or less in the Province of Saskatchewan, Canada in the years 1961-1966 were reviewed and compared with cases in the province in the period 1947-1960, and results were compared with those of other centers. There were 83 cases, giving an incidence of 4.4/100,000 children/yr., and an av. of 13.8 cases/yr.; this was an increase over what was recorded for the previous period and other areas. There was no apparent cause for this increase, and no differences were noted in age distribution, sex or cell type. No geographic clustering was found. Seasonal distribution showed that January and February, with 11 and 10 cases, resp., had the highest number of recorded cases. Mean survival for all cases was 10.7 mo., and for lymphoblastic cases this was 12.7 mo.

70-1378 MORBIDITY RATE FOR MALIGNANT NEOPLASMS IN CHILDREN IN THE BULGARIAN PEOPLES' REPUBLIC DURING THE YEARS 1960-1964. (Ger.) Dontschewa-Stratewa, N. (Br. Paschovi Str. 6, Sofia, Bulgaria). Strahlentherapie 138(4): 410-416, 1969.

The mean annual incidence of new pediatric cases of malignancy (1960-1964, inclusive) was 15.6/100,000 children 14 yr. of age or under; for boys, it was 17.7/100,000; for girls, it was 13.5/100,000. The difference was statistically significant, with a male:female ratio of 1.4:1.0. The absolute incidence, percentage of all tumors represented, and morbidity rate (as above) are tabulated for all children and for boys and girls separately for malignancies at 37 primary sites. Most frequently seen among all children (in descending order; all tabulations = /100,000) were leukemias (4.4), malignancies of the nervous system (cerebral = 3.1; all others = 0-4), lymphoreticulosarcoma (1.5), Hodgkin's disease (1.2) and malignant tumors of the bone (1.0), kidney (1.0) and eyes (0.6). The same order of incidence was obtained for boys alone;

for girls alone, it was leukemia, nervous system malignancies, cancers of the kidney, Hodgkin's disease, lymphoreticulosarcoma, and tumors of the bones and eyes. Leukemia, lymphoreticulosarcoma and Hodgkin's disease accounted for 46% of the malignancies in all children, 49% of those in boys and 41.8% of those in girls. Differences between overall urban and rural morbidity rates or between the overall morbidity rates for various age groups were not statistically significant. In general, morbidity rates in the central provinces were higher than those of the rest of the country, although the increase was not at a level of statistical significance.

70-1379 MALIGNANT TUMOURS OF THE MALE BREAST IN FINLAND. A REPORT OF 51 CASES. (E.) Peltokallio, P. (U. Helsinki 2nd Surg. Clin.) and T. B. Kalima. Brit. J. Cancer 23(3): 480-487, 1969.

Between 1953 and 1963 in Finland there were 51 malignant mammary tumors in males (Finnish Cancer Registry). They comprised 0.54% of all mammary tumors during this period, for an annual morbidity of 0.19/100,000 men. The distribution of tumor types was 42 carcinomas (2 men had bilateral tumors), 3 sarcomas, 2 malignant lymphomas and 4 were unknown. The mean and median age of the 42 pts. with histologically definite carcinoma was 66 yr. ranging from 41-91, with 7 pts. over 80. Male mortality was 0.1/100,000 population during these yr., compared to 0.2/100,000 in the U.S. Heredity, trauma, gynecomastia and hormonal therapy were not found to be factors in genesis of the carcinomas. Prognosis was found to be relatively poor for males as compared to females.

70-1380 CANCER IN FINLAND 1954-1963, (E.) Saxén, E. (Finnish Cancer Registry, Helsinki), M. Hakama and M. Lehtonen. Ann. Clin. Res. 1(4):291-300, 1969.

The incidence of various forms of cancer in Finland during the 10-yr. period 1954-1963 was assessed from data recorded with the Finnish Cancer Registry. During this period the total cancer incidence was 219/100,000 per yr.; for males it was 227/100,000 and for females, 212/100,000. There was an increase in the incidence of lung cancer, from 39 to 65 per 100,000 in men from 1954 to 1963; the incidence among Finnish males was much higher than in other Scandinavian countries. There was a decrease in incidence rates for stomach cancer in both sexes, which was more pronounced in younger age groups. There was an unusual sex ratio (female/male) in g.i. cancer: esophagus, 1.14; stomach, 0.84; colon, 1.62 and rectum, 1.32. There was an upward trend in incidence of registered cases of cancer of the cervix, prostate, bladder and skin, and leukemia, which reflected in part the aging and urbanization of the population. The

overall 5-yr. survival rates for males improved from 22.2 to 23.5 and for females from 35.3 to 36.4 cases diagnosed in 1954 and 1959, resp. The incidence of invasive cancer of the uterine cervix remained stable, but there was a sharp increase in incidence of in situ cases since a screening program was established.

70-1381 THE GEOGRAPHICAL DISTRIBUTION OF MALIGNANT MELANOMA IN QUEENSLAND. (E.) Herron, J. (Princess Alexandra Hosp., Brisbane, Australia). Med. J. Aust. 2(18): 892-894, 1969.

Data concerning 1,100 pts. treated for malignant melanoma in Queensland were analyzed in order to estimate the regional incidence. In 1965 the incidence was 16.4/100,000 population. The state of Queensland is divided into 13 statistical divisions. Distribution was higher in coastal divisions (av., 0.63/1,000 population; range, 0.37-0.77) than in inland divisions (av., 0.55/1,000 population; range, 0.27-0.66). When the areas were subdivided using the Great Dividing Range as an abscissa, the coastal areas showed a distribution of 0.56-0.71/1,000 population, and inland areas had a distribution of from 0.40-0.47/1,000 population. There was little difference between northern, central and southern Queensland, the distribution being 0.63, 0.51 and 0.71/1,000 population, resp. It is suggested that the higher distribution in coastal areas may be related to greater exposure to sunlight.

70-1382 MALIGNANT TUMORS IN CHINESE. A REPORT BASED ON BIOPSY AND AUTOPSY MATERIAL FROM CHINESE IN HONG KONG. (E.) Belamaric, J. (Wayne State U. Sch. Med., Detroit, Mich.). Int. J. Cancer 4(4):560-573, 1969.

A study was done to determine the relative frequency of different forms of cancer among the Chinese in Hong Kong. Of a total of 5,634 solid malignant tumors diagnosed in Hong Kong from January, 1961 - January, 1966, 4934 were found in surgical specimens, for an incidence of 53 new cases/100,000/yr. Cancers from non-Chinese pts. are excluded from this study. In both sexes, the incidence rate increased up to the sixth decade; 56% of all the cancers were found in females, possibly due to sampling factors. In decreasing order of frequency, the most common malignant tumors seen for males were cancer of the nasopharynx, liver, esophagus, stomach and lung, and for females cancer of the cervix, breast, nasopharynx, intestine and stomach. The Chinese population in Hong Kong showed a high incidence of carcinoma of the nasopharynx, liver and chorion, and relative infrequency of carcinoma of the prostate gland and squamous cell carcinoma of the lip. Penile cancer comprised 1.1% of the cancers in men, and is one of the lowest percentages reported for Chinese.

70-1383 HOMOLOGOUS TUMOURS OF THE TESTIS AND THE OVARY. (E.) Bhargava, M. K. (Karnatak Med. Coll., Hubli, India) and S. K. Bhargava. Indian J. Cancer 5(4):291-300, 1968.

During the 12-yr.-period 1947-1959, 67 tumors of the testis and 358 of the ovary were discovered. Ovarian neoplasms were 5 times as common as testicular. While all testicular tumors were malignant, only 100/358 (30.4%) of ovarian tumors were malignant primary tumors. Testicular tumors formed 2.73% of total malignancies in males and ovarian tumors formed 4.35% in females. Only 63/358 (17.6%) of ovarian tumors were germinal, compared to 63/67 (94.3%) of testicular neoplasms. Among testicular tumors, 69.6% occurred in the 20-49 yr. age group. In the ovarian series, 69% were in the 30-39 yr. age group. The av. age at diagnosis was 31.1 yr. and 37.2 yr. for testicular and ovarian tumors, resp. Among testicular tumors, 30/67 (44.8%) were seminoma, 14/67 (21%) embryonal carcinoma, 7/67 (10.4%) teratoma, 11/67 (16.4%) immature teratoma and 1/67 (1.5%) choriocarcinoma. For ovarian tumors, 11/358 (3%) were dysgerminoma, 15/358 (12.56%) teratoma, 5/358 (1.4%) malignant teratoma, and there were 1 each of choriocarcinoma and arrhenoblastoma. The differences in age distribution of ovarian tumors compared to testicular tumors is possibly due to hormonal patterns found in the infant, child, and adult of either sex.

0-1384 SURVIVORSHIP WITH MOUTH AND PHARYNX CANCERS AND THEIR ASSOCIATION WITH CIRRHOSIS OF THE LIVER, MARITAL STATUS, AND RESIDENCE. (E.) Keller, A. Z. (VA Cent. Office, Washington, D. C.). Amer. J. Public Health 9(7):1139-1153, 1969.

20% sample was made of male pts. with histologically-confirmed squamous cell carcinoma of the mouth and pharynx listed in the Veterans Administration Central Office from 1959-1961. Controls for the 706 cases were males matched for age and type of hospital (bed capacity, status with resp. to medical school affiliation). Compared with other medical and surgical patients, cancer patients tended to be treated in larger hospitals affiliated with medical schools. The cases ranged in age from 32-87; 46.2% were between 60-69, and the median age was 63 yr. for cases and controls. Compared to controls, cases in the sample had a higher percentage of divorce (7.1 and 8.1, resp.); they were less likely to be Jews (0.3 and 3.4%, resp.) or to have diabetes mellitus, and were more likely to have cirrhosis of the liver. Survival was not affected by race, religion, marital status, residence, occupation, or by occurrence of cirrhosis of the liver, syphilis, rheumatoid arthritis, diabetes, or various neoplasms. Small, localized lesions had the best prognosis.

70-1385 BREAST CANCER AND REPRODUCTIVE HISTORY OF WOMEN IN SOUTH WALES. (E.) Lowe, C. R. (Dept. Social Occupat. Med. The Parade, Cardiff, Wales) and B. MacMahon. Lancet 1(7639):153-157, 1970.

New cases of breast cancer occurring in South Wales during a 2-yr. period starting May 1, 1965 were compared to hospital controls (619 and 1826, resp.). The cancer pts. were of a higher socioeconomic status, those with 16 or more yr. of schooling having a risk 3 times that of pts. with 12 yr. of schooling or less. Married women were of a lower relative risk, as compared to 61 cases of those women never married (44.3 expected). An inverse relationship was observed between breast cancer and number of full-term pregnancies; nulliparous females had 3 times the risk of those with 5 full-term pregnancies. This was not due to lactational experience. Females married for the first time after age 30 yr. had 3 times the risk of those married when under 20 yr., probably because of an earlier first pregnancy.

70-1386 DISTRIBUTION MAPS OF ESOPHAGEAL CANCER AMONG BANTU IN THE TRANSKEI. (E.) Burrell, R. J. W. (Rhodes U. Bantu Cancer Chem Res. c/o N. R. C., Butterworth, Transkei, South Africa). J. Nat. Cancer Inst. 43(4):877-889, 1969.

A survey was made in 1955-1959 of esophageal cancer among the South African Bantu in the Transkei (population about 1.6 million). A total of 1,036 males and 846 females with possible cancer of the esophagus were found, about 20% of which were confirmed by radiologic and histologic signs, 40% by radiological signs only, and 40% by clinical description. The death rates from this disease were higher in females than males until age 50, when the female rates leveled off, while the male rates continued to increase greatly until age 60. The site of the cancer was most often in the middle third of the esophagus with a tendency to be in the lower third in the older people. Many of the older Bantus claim that this disease was unknown 25 yr. before. Maps are presented charting the distribution of esophageal cancer according to sex in this area.

70-1387 PREVALENCE RATES OF UTERINE CERVICAL CARCINOMA IN SITU FOR WOMEN USING THE DIAPHRAGM OR CONTRACEPTIVE ORAL STEROIDS. (E.) Melamed, M. R. (Memorial Hosp. Cancer Allied Dis., New York, N. Y.), L. G. Koss, B. J. Flehinger, R. P. Kelisky and H. Dubrow. Brit. Med. J. 3(5664):195-200, 1969.

The prevalence rates of cervical carcinoma in situ were compared in women attending

- 70-1393 POLYPOIDY IN MALIGNANT MELANOMA. (E.) Whang-Peng, J. (NCI, Bethesda, Md.), P. Chretien and T. Knutsen. Cancer 25(5): 1216-1223, 1970.

Case histories and chromosomal studies on 6 pts. with malignant melanoma are reviewed. All had aneuploid cell lines, either hyperdiploid, nearly triploid, tetraploid or hypertetraploid, but only 2 had definite stem-cell lines, the others having too wide a distribution. Marker chromosomes, large submetacentrics and long acrocentrics, were seen in 3 cases. Only one case was studied from the primary lesion, the others either from metastatic lesions, lymph nodes or effusions. It was thought that continuous replication defects and mitotic abnormalities may contribute to the rapid growth of this neoplasm.

- 70-1394 Xg LOCUS: FAILURE TO DETECT INACTIVATION IN FEMALES WITH CHRONIC MYELOCYTIC LEUKAEMIA. (E.) Fialkow, P. J. (U. Washington, Seattle), R. Lisker, E. R. Giblett and C. Zavala. Nature (London) 226(5243):367-368, 1970.

In 37 women with typical chronic myelocytic leukemia (CML), 26 (including 2 children) had the Philadelphia (Ph^1) chromosome. Only 2/37 were typed as Xg(a-), and both had the Ph^1 chromosome. Of 35 typed as Xg(a+), 11 were thought to be Xg^a/Xg heterozygotes; 8/11 tested had the Ph^1 chromosome. CML or its therapy probably does not change the Xg phenotype from Xg(a-) to Xg(a+), since 2 of the Ph^1 -positive pts. treated with busulphan were Xg(a-), 3/13 males with CML were Xg(a-) and no discrepancies in Xg inheritance were found in 39 families studied (30 families of female and 9 of male pts.). It is concluded that either the Xg locus does not undergo random fixed inactivation in CML red cells and possibly in red cells in general, or that the Xg^a antigen is not synthesized in the red cells themselves.

- 70-1395 CHROMOSOME CONSTITUTION OF CARCINOMA OF THE ENDOMETRIUM. (E.) Tseng, P.-Y. (Johns Hopkins U. Sch. Med., Baltimore, Md.) and H. W. Jones, Jr. Obstet. Gynec. 33(6):741-752, 1969.

Chromosomal studies were made on tissues from 7 cases of adenocarcinoma of the endometrium. Aneuploid cells were found in all cases, but in contrast to ovarian and cervical cancers, there was a large number of euploid cells with apparently normal karyotypes (10/12 diploid cells in one case, 10/13 in another). It is unknown whether these cells have a more subtle structural difference, are from normal stroma or are from normal gland cells existing among the neoplastic ones.

- 70-1396 CHROMOSOME ANALYSIS IN A PROGRESSIVE LESION OF THE CERVIX. (E.) Stanley,

M. A. (Queen Elizabeth Hosp., Woodville, Australia) and J. A. Kirkland. Acta. Cytol. (Balt.) 13(2):76-80, 1969.

A cervical lesion in a 35-yr.-old woman, appearing to be a dysplasia, was punch biopsied and a chromosomal count of the cells yielded 1 accurate count of 45, 27 counts ranging from 46-50, and a small population of 63-65 and 64-68. A diagnosis of severe dysplasia was made 9 mo. later and only one accurate count of 42 was made. Another biopsy indicated carcinoma *in situ* and the pattern of distribution of the chromosomes was like that of the first. After another 6 weeks, a hysterectomy was performed and 44% of the cells were found to have a chromosomal count of 46. Analysis of 7 of these cells showed 1 with a normal female karyotype and 6 that were pseudodiploid (loss in groups A and B, and an addition in E and F). Analysis was also made on 1 hypodiploid and 3 hyperdiploid cells.

- 70-1397 CORRELATION BETWEEN THE Gc-TYPE AND DIFFERENT FORMS OF LEUKEMIA. (Ger.) Gurda, M. (Med. Acad. 3rd Med. Clin., Cracow, Poland). Folia Haemat. (Leipzig) 91(4):452-456, 1969.

Statistical analysis of Gc phenotypes determined in 52 pts. with acute myeloblastic, 45 chronic granulocytic and 78 lymphatic leukemia revealed no differences between leukemic patients and healthy population, no correlation between age and sex and Gc type in leukemic patients and no correlation between Gc type and different forms of leukemia. The distributions were 44.77%, 45.93% and 9.30% for Gc type 1-1, 2-1 and 2-2, resp., in leukemia and 43.62%, 45.40% and 10.98%, resp., in the healthy population (according to the study of Kobiela *et al*).

- 70-1398 Xg BLOOD-GROUPS AND CLONAL-ORIGIN THEORY OF CHRONIC MYELOID LEUKAEMIA. (E.) Lawler, S. D. (Roy. Marsden Hosp. Inst. Cancer Res., London) and R. Sanger. Lancet 1(7647):584-585, 1970.

The Xg groups of 48 female pts. with chronic myeloid leukemia, all having the Philadelphia chromosome (Ph^1), were those expected from females, and were significantly different from a male distribution. This result may be interpreted to mean either that the Xg locus, when on a presumably normal X, is not subject to inactivation, or that the theory that all the Ph^1 -positive cells represent a single clone is not valid. If the clonal theory is correct Xg is not inactivated: if Xg is inactivated, the clonal theory is incorrect.

- 70-1399 INTERACTION OF CHROMATID BREAKS INDUCED BY NITROSOGUANIDINE IN COMBINATION WITH

SOME RADIOMIMETICS AND X-RAYS. (E.) Kaul, B. L. (Max Planck Inst. Reproduct. Res., Cologne-Vogelsang, Germany). Chromosoma 26(4):469-474, 1969.

Lateral roots of Vicia faba (about 1 cm long) were treated with soln. of 0.0075% nitrosoguanidine (NG) alone or in combination with 0.001% diepoxybutane (DEB), 0.3% ethylmethane sulfonate (ES), or 0.005% ethyleneimine (EI) at 22° C for various durations, then placed in tap-water for 24-48 hour, and treated with 0.05% colchicine for 3 hours. The number of isochromatid breaks per cell was higher than additive in each case except NG + EI. Observation of chromatid interchanges indicated a complete interaction of breaks induced by NG in combination with DEB, ES, or EI, suggesting that these breaks are of a similar nature. However, chromatid breaks induced by NG followed by X-rays (600 r) had an additive effect but no interaction for interchanges. It is believed that these breaks are either dissimilar in nature or not synchronized with respect to time.

70-1400 KLINEFELTER'S SYNDROME AND CANCER OF THE BREAST. (E.) Cuenca, C. R. and K. L. Becker (50 Irving St. NW, Washington, D. C.). Arch. Intern. Med. (Chicago) 121(2):159-162, 1968.

A 63-yr.-old Negro male, who had a serosanguineous discharge for 2 weeks from the right breast, was examined. Bilateral gynecomastia was present since adolescence, pubic and axillary hair appeared at age 19, and libido and potencia were normal until age 58, when they decreased markedly. Urinary estrogens were normal. A chromatin-positive buccal smear and testicular biopsy were characteristic for Klinefelter's syndrome. Excisional biopsy of the right breast revealed both gynecomastia and carcinoma. Cancer of the breast is 100 times less in males than females, and about 1/400 males have Klinefelter's syndrome. In the 6 pts. reported with both, all had cancer of the right breast, whereas cancer of the breast in men is slightly more common in the left. Some evidence of gynecomastia was seen in all 6 pts.

0-1401 CARCINOMA OF PENIS ARISING FROM LATE BENIGN SYPHILIS - CASE REPORT. (E.) Wittken, J. (70 Convent Ave., New York, N. Y.) and J. C. Pellin. Cutis 5(6):695-699, 1969.

46-yr.-old Negro reported to the hospital because of a rapidly-growing lesion of the penis. It began as a small hard 'pimple' 7 mo. before that, would itch but was not painful, and now appeared as a large, fungating, papillary, friable, grey-white mass, measuring 5 cm. in max. dimensions. He had been circumcised at 9 yr. of age and had never been treated for venereal disease. The end of his penis had become hard and bumpy in the last few yr. but caused no discomfort. The Venereal Disease Research Laboratories tests

for syphilis were positive undiluted, and the fluorescent treponemal antibody absorption test was reactive. There were no signs of tertiary syphilis. Biopsy of the penile growth disclosed squamous cell carcinoma.

70-1402 BLASTIC RESPONSE OF LYMPHOCYTES IN MOSAIC DOWN'S SYNDROME UNDER SERIAL PHA DILUTIONS. (E.) Matte, R. (Hokkaido U. Zool. Inst., Sapporo, Japan), M. Sasaki and Y. Obara. Jap. J. Hum. Genet. 14(2):160-162, 1969.

Blood from a 20-yr.-old male pt. with clinical and dermatoglyphic signs characteristic of atypical Down's syndrome was incubated for 3 days in serial dilutions of phytohemagglutinin (1-0.78%). Blood and skin cultures demonstrated a mosaic state, with the trisomic line representing 5-6% of the mitoses. The percentage of blast transformation and mitosis of lymphocytes (at least 150 cells from each dilution were counted and 100 karyotypes of the mosaic case analyzed) was intermediate between that of a normal 6-yr.-old male and one demonstrating pure trisomy. The percentage of trisomic cells remained consistent through the entire serial dilution.

70-1403 SEX CORD TUMOR WITH ANNULAR TUBULES. A DISTINCTIVE OVARIAN TUMOR OF THE PEUTZ-JEGHERS SYNDROME. (E.) Scully, R. E. (Massachusetts Gen. Hosp., Boston). Cancer 25(5):1107-1121, 1970.

A review of 10 pts. with a rare ovarian tumor revealed 3 cases associated with Peutz-Jeghers syndrome. The tumors were multifocal within the ovarian stroma and were composed of rounded epithelial nests containing eosinophilic hyaline bodies with faint laminations and lipid vacuolization. The epithelial nests formed simple or complex annular tubules and calcification was common. The tumor is believed to arise from granulosa cells, but similarities to a Brenner tumor, Sertoli-cell tumor and gynandroblastoma have also been noted. The most appropriate designation was a "sex cord tumor with annular tubules". Examination of microscopic slides of 10/12 ovarian tumors reported in association with this syndrome, revealed 3 additional cases of this neoplasm.

70-1404 SARCOMA AT THE SITE OF PREVIOUS TRAUMA IN PAGET'S DISEASE. (E.) Semple, J. C. (U. Oxford, England). Postgrad. Med. J. 45(529):740-742, 1969.

Paget's disease of the left humerus and scapula was discovered in a 61-yr.-old carpenter who complained of pain in the left shoulder following a fall. The surgical head of the left humerus was fractured 4 yr. later when he fell down some stairs, but it healed well within 3 mo. After about 10 yr., during which he suffered occasional

Planned Parenthood Centers using the diaphragm (6,809) and using oral steroids (27,508) in a study from October, 1965-July, 1967. In all, there was one case of invasive carcinoma, 14 carcinomas in situ with microfocal invasion and 192 carcinoma in situ. The prevalence of cervical carcinoma was significantly higher in women using steroid contraceptives even after corrections were made for age, ethnic origin, age at first pregnancy (early sexual experience), number of live births and family income.

70-1388 INTERPRETATION OF THE VITAL STATISTICS OF BREAST CANCER. (E.) Feinleib, M. (Nat. Heart Inst., Bethesda, Md.) and R. J. Garrison. Cancer 24(6):1109-1116, 1969.

Mortality rates for breast cancer in the United States in 1960-1966 (inclusive) showed a sharp increase during the reproductive yr., with a slower increase after age 55, while statistics from Japan, Yugoslavia and Finland showed a comparable increase up to age 45, followed by lower constant rates. Incidence rates for breast cancer in Connecticut increased about 45% among females less than 55 yr. (comparing the 1935-1939 and 1960-1964 rates), and were unchanged for females older than 55 yr. Mortality rates increased only 25% relative to the increase in incidence in women under 55. Racial and regional differences were related to the frequency and quality of ovarian function which may be influenced by such factors as nutrition, fertility and genetic factors.

70-1389 FEMALE SUSCEPTIBILITY TO CANCER AND OTHER DISEASES AS INDICATED BY BRITISH AND EUROPEAN MORTALITY RATES. (E.) Stocks, P. (34 Brompton Ave., Colwyn Bay, North Wales). Brit. J. Cancer 23(2):254-268, 1969.

The female/male (F/M) ratio of cancer of the thyroid in England and Wales, 1950-1963, varied from 1.5-3.4 at different ages, but was usually 2.2, dropping to about 1.7 at ages 45-60. An excess of females with cancer of the thyroid was also seen in countries of northern Europe as opposed to mid-Europe. The F/M ratio of cancer of the biliary passages in England and Wales, 1963-1966, was 1.3 after age 40, although cancer of the liver was more often seen in males. However, in Ireland, the Netherlands, German Federal Republic and Austria, the F/M ratio for primary cancer of the liver was greater than 1.0. No excess of females was seen with cancer of the pancreas or rectum, but in England, Wales and other countries of northern Europe, the F/M ratio for cancer of the intestines up to age 54 was 1.2. The F/M ratio for malignant melanoma at age 35-40 was 1.27, but overall skin cancer was higher in males.

70-1390 CARCINOMA AND INTESTINAL METAPLASIA OF THE STOMACH IN COLOMBIAN MIGRANTS.

See also abstract nos.: 990,992,994,1004,1014,1016,1024,1027,1102,1117,1118,1121,1122,1123,1136,1225,1255,1256,1397,1400,1406,1420,1431,1432

(E.) Correa, P. (U. Valle Sch. Med., Cali, Colombia), C. Cuello and E. Duque. J. Nat. Cancer Inst. 44(2):297-306, 1970.

Histologic specimens were obtained at autopsy from persons who had died of violent and natural causes in Cali, Colombia from 1966-1968. The incidence of gastric carcinoma of the intestinal type in the various migrant groups was highest for all age groups and both sexes in the migrants from the south. This was not true for the diffuse type of gastric carcinoma. A strong positive correlation was found in the incidence of intestinal metaplasia and gastric carcinoma of the intestinal type; the possibility of this being a premalignant lesion was discussed.

70-1391 DACTYLOSCOPIC PATTERNS (DERMATOGLYPHS) IN PATIENTS WITH LEUKEMIA. (Pol.) Aleksandrowicz, J. (3rd Intern. Dis. Clin., Cracow, Poland), T. Debski and Z. Schiffer. Pol. Arch. Med. Wewnet. 43(1):991-998, 1969.

Significant differences were observed in dactyloscopic patterns from 250 pts. (155 men, 95 women) with various types of leukemia and from 600 healthy controls. Radial loops were seen more frequently in men with leukemia (47%, regardless of type) than healthy controls (29%), and radially directed swirls were seen more frequently in women pts. (43%) than healthy women (29%). Radial loops were present in 60% of men with chronic granulocytic and 43% of men with chronic lymphocytic leukemia (as compared to 29% in healthy controls), while radial swirls were present in 42% and 52% of women, resp. (as compared to 29% in healthy women). Since dactyloscopic patterns are established before the fourth mo. of fetal life, it is suggested that any chromosomal aberration caused by a leukomogenic effect expressing itself in an alteration of dermatoglyphs must take place before then. The study of dermatoglyphs for possible detection of leukemia-predisposed persons is recommended.

70-1392 SOLAR ACTIVITY AND INCIDENCE OF LEUKEMIA. (Pol.) Aleksandrowicz, J. (3rd Intern. Dis. Clin., Cracow, Poland), K. Janicki, M. Gurda and Z. Schiffer. Pol. Tyg. Lek. 24(21):797-799, 1969.

A statistical study revealed a weak, but significant, positive linear correlation between the incidence of leukemia between 1951-1960 (120 mo.) expressed by the monthly index of hospitalized new cases of leukemia /100,000 population in the Cracow area and solar activity expressed in mean monthly Wolff numbers. The significance of this correlation increased when the solar activity 12 mo. preceding hospitalization was used in the calculations, and decreased when the solar activity from 24 preceding mo. was used. The possible influence of cosmic factors on stimulation of carcinogenesis is briefly discussed.

backaches due to his progressing Paget's disease, he presented with pain and swelling of the left shoulder. His head was enlarged, he had bowing of the tibia and dorsal kyphosis. Biopsy of the shoulder revealed an osteogenic sarcoma invading the deltoid muscle.

70-1405 MYELOID LEUKEMIA IN HODGKIN'S DISEASE: CHROMOSOMAL ABNORMALITIES. (E.) Ezdinli, E. Z. (Roswell Park Mem. Inst., Buffalo, N. Y.), J. E. Sokal, C. W. Aungst, U. Kim and A. A. Sandberg. Ann. Intern. Med. 71(6):1097-1104, 1969.

Case reports of 3 pts. with Hodgkin's disease, later developing myeloid leukemia (acute myeloblastic, chronic myelocytic, and erythroleukemia) are presented, and chromosomal analysis of bone marrow cells showed abnormalities indicative of the respective leukemias. No aneuploidy was noted in any of 28 pts. with Hodgkin's disease alone. All the described pts. and 4/5 similar cases reported elsewhere received radiation therapy, with a median latent period between the radiation treatment and the onset of myeloid leukemia of 1 yr.

70-1406 MONGOLISM AND LEUKEMIA. CLINICAL AND CYTOGENETIC FINDINGS IN FOUR MONGOLOID CHILDREN WITH LEUKEMIA. (Ger.) Hellriegel, K. (Univ. Med. Clin., Cologne-Lindenthal, Germany), J. A. Pfeiffer, R. Seiler, C. Schütz and H. J. Wickers. Munchen. Med. Wschr. 111(29):1522-1528, 1969.

Four mongoloid children (2 boys, 2 girls; aged 5 yr.) developed acute lymphoblastic (2/4) or stem-cell (2/4) leukemia. In 2/4, chromosomal findings failed to deviate significantly from the usual constitutional karyotype for mongoloid children: trisomy 21+, with a majority of mitoses showing 47 chromosomes. However, 1/4 showed occasional mitoses with 48 chromosomes and 1/4 showed numerous mitoses with 48 or 49. In all cases, mitoses with less than 47 chromosomes showed an absence of various, rather than specific, chromosomes. Case histories are presented.

70-1407 THE CHEDIAK-HIGASHI SYNDROME: CONTINUOUS SUSPENSION CULTURES DERIVED FROM PERIPHERAL BLOOD. (E.) Blume, R. S., P. R. Wade, H. R. Gralnick, L. N. Chessin, A. T. Haase and S. M. Wolff (NIH, Bethesda, Md.). Blood (6):821-832, 1969.

Three long-term suspension cultures were established from peripheral blood WBC, 2 from a 7-yr.-old male pt. in the accelerated phase of the Chediak-Higashi syndrome (homozygous lines) and from his father (heterozygous line). Cells in these lines were principally lymphoblastoid in appearance, synthesized immunoglobulins and

interferon, and had a modest phagocytic capacity (38% of cells from the homozygous line and 14% from the heterozygous line had phagocytic activity.) Giant abnormal granules characteristic of the syndrome were present in the homozygous lines; abnormally large granules were also present in the heterozygous line. The lysosomal nature of these granules was demonstrated by histochemical and supravital staining. Striking Golgi zone prominence was found in the heterozygous line, and was also present to a less degree in the homozygous lines.

70-1408 PHEOCHROMOCYTOMA WITH RENAL ARTERY COMPRESSION IN AN IDENTICAL TWIN. (E.) Kerzner, M. S. (VA Hosp., Providence, R. I.), J. A. Reeves, D. DeNyse and B. C. Claunch. Arch. Intern. Med. (Chicago) 121(1):91-94, 1968.

A 47-yr.-old male was admitted to the hospital because of sudden left hemiparesis. During the previous yr., he had become more easily fatigued, was conscious of a forceful heartbeat, and experienced frequent headaches and drenching sweats. He had been treated for hypertension since the age of 16, but had an identical twin brother who was normotensive and asymptomatic to date. Renograms and aortography indicated a stenosis of the right renal artery, which upon surgical correction, was found to be compressed by a pheochromocytoma. The pt. has been normotensive for 3 yr. following excision of the tumor and nephrectomy. A similar case in a 32-yr.-old woman is discussed. Pheochromocytoma has been reported in about 0.5% of the hypertensive population.

70-1409 METANEPHRIC HAMARTOMAS AND NEPHROBLASTOMATOSIS IN SIBLINGS. (E.) Liban, E. (Beilinson Hosp., Petah Tiqva, Israel) and I. L. Kozenitzky. Cancer 25(4):885-888, 1970.

A male infant, the second child of a 21-yr.-old Yemenite female was born at term with signs of asphyxia and died of respiratory distress within 48 hr. Histological examination of the kidneys revealed a number of areas of primitive metanephric tissue throughout the cortex, consisting of small foci of round or oval hyperchromatic cells without recognizable cytoplasm. There were no distinct signs of a neoplastic process and they were considered to be multiple metanephric hamartomas. The kidneys of a fourth child, a female stillborn about 2.5 yr. later, had foci of metanephric tissue similar to the hamartomas of the other child, and also diffuse, extensive involvement of both kidneys with structures similar to a Wilms' tumor. This was diagnosed as congenital, bilateral, diffuse nephroblastomatosis.

70-1410 REGIONAL ENTERITIS LEADING TO CARCINOMA OF THE SMALL BOWEL. (E.)

Wyatt, A. P. (Mem. Hosp., Woolwich, London). *Gut* 10(11):924-927, 1969.

A 33-yr.-old male was examined with a history of severe diarrhea, his first attack occurring 7 yr. before and lasting for 3 mo. He was wasted, anorexic, with vague abdominal pain and borborygmi, but reported no blood or mucous in the stool. A surgical procedure was performed for correction of an iliorectal fistula, discovered by barium enema, and a section of the terminal ileum appeared thickened and fibrotic with a distended section showing gross cobblestone changes, ulceration and pseudopolyps. Acinar adenocarcinoma was seen in some areas of the mucosa with extension into the subserosal fat. Adenocarcinoma of the small intestine associated with Crohn's disease was reviewed in 16 other cases with a mean duration of bowel symptoms of 15.7 yr. and an av. age at diagnosis of malignancy of 42.7 yr.

70-1411 A CLINICAL STUDY OF THE PSYCHOSOMATIC ASPECTS OF CANCER. (E.) Tenney, V. A. *Asian Med. J.* 11(12):16-21, 1968.

A psychiatric study was made of 135 pts. diagnosed as having cancer, and a specific personality pattern noted. The pts. seemed to have a secret self-loathing, which was masked, even to themselves, by a self-image supported by an emotional relationship with another person or by a respected position in society. When this image was destroyed, either by removal of the person through which he expressed himself, or loss of his position, this self-hatred became manifest and the pt. did not consider himself anything worth living for. This may, possibly through hormonal mechanisms, accelerate the progress of cancer to a fatal end. Several case histories are presented.

70-1412 PSYCHOENDOCRINE ASPECTS OF CANCER OF THE BREAST. (E.) Katz, J. L. (Montefiore Hosp. Med. Ctr., Bronx, N. Y.), P. Ackman, Y. Rothwax, E. J. Sachar, H. Weiner, L. Hellman and T. F. Gallagher. *Psychosom. Med.* 32(1):1-18, 1970.

Psychiatric interviews were made on 30 women (6 Negro, 2 Puerto Rican and the rest white) prior to biopsy of a breast tumor in order to assess their ego defenses and correlate them with daily hydrocortisone production, urinary hydrocortisone and androgen metabolites. The rank order correlation between the scores for extent of defensive failing and production of hydrocortisone was 0.48 (p below 0.02) and for excretion of metabolites (tetrahydrocortisone, tetrahydrocortisol, and allotetrahydrocortisol) 0.38 (p below 0.05). Considering only the 22 women whose tumors were malignant, the correlation was 0.50 (p below 0.02) and 0.49 (p below 0.02), resp. Scores from a single interviewer were more accurate than interviewer analysis of the taped interview, and affect was the best "predictor" of hydrocortisone pro-

duction rate. There was no correlation with androgen metabolites.

70-1413 SOMATIC VARIATION AND MULTIPLE NEUROFIBROMATOSIS. (E.) Nicholls, E. M. (U. New South Wales Sch. Human Genet., Sydney, Australia). *Hum. Hered.* 19(5):473-479, 1969.

A study of 32 pts. (7 cases presented) with neurofibromatosis was made correlating the familial pattern and occurrence of freckles and other abnormally pigmented areas (café au lait spots). Most cases were indicative of dominant inheritance, represented by the genotype 'Nn', which was also thought to cause an increase in freckles and pigmented patches, but no further change in the melanocytes. Randomly distributed lesions of the pigmentary and nervous systems increased with age and were usually unrelated, but in several cases, plexiform neuromata were seen in a related pigmented area. The possibility of mutation as an initiating factor is discussed.

70-1414 FURTHER OBSERVATIONS ON SPONTANEOUS BLASTOID TRANSFORMATION OF HUMAN SMALL LYMPHOCYTES IN VITRO. (E.) Caron, G. A. (U. Oregon Med. Sch., Portland). *Brit. J. Haemat.* 16(3):313-322, 1969.

Synthesis of DNA, measured by tritiated thymidine uptake during the final hour *in vitro*, was used as a measure of blast transformation of human peripheral small lymphocytes cultured in media containing 20% autologous plasma; an av. of 0.08% (range, 0-0.32%) of the mononuclear cells surviving on the sixth day were then synthesizing DNA and could incorporate the thymidine. In control cultures of more than 6 days duration from 1 of 2 subjects, a larger proportion of mononuclear cells became labeled with tritiated thymidine (av. 0.57%; range, 0.14-1.3%). In 3 control cultures of only 3 days duration, 0-0.04% of labeled cells (av. 0.01%) were found. Spontaneous transformation was consistently low for up to 6 days, and thereafter there was a relatively slight increase. Critical evaluation of previous reports of spontaneous lymphocyte transformation suggested that this is minimal when the cells are cultured in autologous plasma and that heterologous sera may act as an unsuspected transformation stimulant.

70-1415 A CASE OF BIERMER'S ANEMIA WITH CIRRHOSIS OF THE LIVER. (DEVELOPMENT FOLLOWED OVER A PERIOD OF 14 YEARS, WITH DEATH DUE TO CARCINOMA OF THE LIVER). (Fr.) Olmer, J. and J.-J. Moutaffian. *Marseille Med.* 106(4):345-348, 1969.

Fourteen yr. after clinical recovery from an alcohol-induced, hypertrophic cirrhosis of the liver, accompanied by pernicious anemia, an 84-yr.-old woman with continuing hepatomegaly + mild diabetes presented with sclerotic hepatitis, recurrent, acute cirrhosis + ascites, and a

learily differentiated carcinoma of the right lobe of the liver, metastasized to the pancreatic lymph nodes. Death due to malignant cirrhosis followed in 2 mo. This development of a carcinomatous, primary neoplasm in cirrhotic liver tissue is considered typical of a carcinogenic sequence which has been reported more and more frequently as the evolution of alcohol-induced cirrhoses has been prolonged increasingly in recent yr.

1416 INABILITY OF PLASMA FROM PATIENTS WITH NEOPLASIA TO SUPPORT MACROPHAGE RECOGNITION OF FOREIGNNESS. (E.) Pisano, J. C. (Emory U. Sch. Med., New Orleans, La.), N. R. Luzio and N. K. Salky. Nature (London) 6(5250):1049-1050, 1970.

Cells were derived from 4 control subjects, 4 pts. with carcinoma (lung, liver, colon, metastatic) and 4 pts. with diabetes, hepatitis, emphysema and aortic aneurysm, and opsonic activity was determined by phagocytic uptake of gelatinized test lipid emulsion by rat liver slices incubated for 30 min. at 37° C. in appropriate solution of serum and heparin. In 17% human serum derived from pts. with carcinoma, rat liver slices phagocytosed 40% less lipid emulsion than with 17% normal human serum; higher conc. of serum from these pts. had no significant effect on the degree of phagocytosis, denoting a profound loss of plasma opsonic activity. Serum from pts. with non-cancerous diseases showed essentially normal opsonic activity. Although the relationship between neoplasia and alterations in opsonin activity is not clear, it is thought that the foreignness of tumor cells and therefore their antigenicity is not recognized by host macrophages.

1417 SQUAMOUS CELL CARCINOMA ARISING IN HIDRADENITIS SUPPURATIVUM. (E.) Humphrey, L. H. (Emory U. Sch. Med., Atlanta, Ga.), H. Playforth and U. W. Leavell, Jr. Arch. Surg. (Chicago) 100(1):59-62, 1969.

A 48-yr.-old white male had a history of abscesses over the axillae, lower gluteal region and intergluteal region for 7 yr. had a cauliflower lesion in the midline between the coccyx and the lumbosacral joints 8 mo. previously, which was excised 2 mo. later. The wound eventually broke down, and after unsuccessful treatment for fungus, a biopsy revealed squamous cell carcinoma.

1418 CHARACTERISTICS OF NORMAL AND MALIGNANT HUMAN MESOTHELIAL CELLS STUDIED IN VITRO. (E.) Castor, C. W. (U. Michigan, Ann Arbor) and B. Naylor. Lab. Invest. 20(5):437-44, 1969.

Cells from the pleural fluids of 4 persons with diffuse pleural mesothelioma were isolated and grown in tissue culture. Their microscopic appearance prior to culture was similar to the normal cells (from the pericardial fluid of 5 heart-surgery patients), with occasional fibroblastic cells and a few multinucleated giant cells. In culture, the mesothelioma cells appeared as continuous strands with collagen-like deposits in between. Chromosome studies showed one strain with significant polyploidy and which had at least 10.5% aneuploid cells. Production and viscosity of hyaluronic acid could not be distinguished from that of normal cells. Growth rates were also similar, the av. generation times ranging from 60 - 150 hours.

1419 AN ELECTRON MICROSCOPE STUDY OF A PIGMENTED TUMOUR OF THE JAW OF INFANTS. (E.) Hayward, A. F. (Roy. Dent. Hosp. Sch. Dent. Surg., London), B. W. Fickling and R. B. Lucas. Brit. J. Cancer 23(4):702-708, 1969.

Electron microscopic examination of a pigmented tumor of the maxilla of a 7-week-old female showed epithelial-like pigmented cells close together, sometimes connected by desmosomes, and with microvillous processes projecting into the intercellular spaces. The cytoplasm of these cells was complex, containing electron-dense, round or spindle-shaped pigment granules directly related in amount to the granular endoplasmic reticulum (ER). The non-pigmented cells were close-packed in groups with a clear space around each mass. They had a large nucleocytoplasmic ratio, no desmosomes and no intercellular projections. The chromatin was distributed peripherally in the nucleus and the cytoplasm was full of ribosomes and polysomes with a few strands of granular ER. An intermediate type of cell may have been seen.

1420 THE KINETICS OF CELLULAR PROLIFERATION IN NORMAL AND MALIGNANT TISSUES. II. AN IN VITRO METHOD FOR INCORPORATION OF TRITIATED THYMIDINE IN HUMAN TISSUES. (E.) Fabrikant, J. I. (Johns Hopkins U. Sch. Hyg. Public Health, Baltimore, Md.), C. L. Wissemann, III and M. J. Vitak. Radiology 92(6):1309-1320, 1969.

An in vitro method for the study of kinetics of cellular proliferation in normal and neoplastic tissues is described, based on a method in which surgical and biopsy specimens are labeled with tritiated thymidine (TdR-³H) in vitro, but under conditions in which the incorporation of the label occurs only in cells which were synthesizing DNA in vivo. The resultant nuclear labeling allows identification of sites of cellular proliferation and provides information on the proliferative capacity of the cell population; in vitro incorporation of TdR-³H results in a

pattern of labeling similar to that obtained by *in vivo* methods. Tissue specimens are incubated in agitated Medium M-199, Earle base, with 20% fetal calf serum and TdR-³H in a specially designed hyperbaric O₂ chamber at 37.5°, pH about 7.5, 2,280 mm Hg pO₂ for 1 hour; percentage labeling indexes and mean grain counts are determined and compared with animal tissues labeled *in vivo*. The experimental results are used to define the characteristics of the standardized *in vitro* method for the quantitative determination of TdR-³H incorporation in human tissue samples.

70-1421 DIFFERENTIATION OF NORMAL AND MALIGNANT CELLS. (E.) Pierce, G. B. (U. Colorado Med. Ctr., Denver). Fed. Proc. 29(3):1248-1254, 1970.

Based on experiments using cloning, isotope tracer and electron-microscopic technics, and employing testicular teratocarcinomas, squamous cell carcinomas of the skin of rats and testicular seminomas, the premise was developed that stem cells of malignant tumors differentiate. This observation is compatible with the notion that the target in carcinogenesis is the normal stem cell of the particular tissue, and that the lesion produced by carcinogenesis is a change in the controls governing the expression of differentiation by malignant stem cells. In cloning experiments, single embryonal carcinoma cells transplanted in the intraperitoneal cavity of mice grew into teratocarcinomas containing 12-15 somatic tissues, and it is concluded that stem cells of 1 cancer could differentiate. Undifferentiated stem cells of squamous cell carcinoma differentiated into mature-appearing squamous pearls.

70-1422 DIFFERENCES IN ENDOPLASMIC RETICULUM IN EPIDERMAL CELLS OF A SKIN-TUMOR-SUSCEPTIBLE AND A SKIN-TUMOR-RESISTANT MOUSE STRAIN. (E.) Stjernvall, L. (U. Helsinki). Ann. Med. Intern. Fenn. 47(4):249-252, 1969.

Electron microscopic examination of epithelial cells from the dorsal skin of 3-mo.-old, female skin-tumor-susceptible (s.t.s.) CF 1 Swiss and skin-tumor-resistant (s.t.r.) RA mice was made in regard to the structure of the endoplasmic reticulum (ER). In the s.t.s. mice the ER appeared well-differentiated; in a long continuous formation in single section; and 3-dimensional in serial section, like flattened convex cisternae. In the s.t.r. mice, the ER had a scattered irregular arrangement; appearing in single section as short canals irregularly spaced; and as a short tubular system in serial section. Ultrastructurally, in both cases the ER was of the granular type with an optically empty matrix.

70-1423 TRANSFORMATION CAPABILITY OF LYMPHOCYTES FROM BLOOD AND SPLEEN IN

LYMPHADENOSIS. (Ger.) Heine, K.-M. (1st Med. Charity Clin., Berlin), H. Stobbe and Z. D. Petrow. Z. Ges. Inn. Med. 24(16):523-526, 1969.

The number/μl blood and percentage of transformed lymphocytes after stimulation with phytohemagglutinin (PHA), streptolysin O (SLO) and tuberculin (PPD) was determined in the blood from 33 pts. with chronic lymphatic leukemia before and after irradiation of spleen or cytostatic therapy and compared to normal values. In untreated pts. the percentage of transformable lymphocytes was lower (because of an increase in immunologically incompetent lymphocytes) (12% after PHA, 6% after SLO and 3% after PPD) than in normal subjects (82%, 34% and 15%, resp.). After therapy the percentage rose to 40%, 34% and 20%, resp.). This increase of relative values was not accompanied by a parallel increase in absolute values. The absolute lymphocyte transformation values were 4,460/μl, 1720/μl and 370/μl, resp., before therapy, 6500/μl, 2800/μl and 1250/μl resp. after therapy and 1490/μl, 645/μl and 290/μl in controls. Transformation of lymphocytes obtained from the spleens of 4 pts. was (after PHA stimulation) either equal to (2 cases) of significantly lower (2 cases) than that of blood lymphocytes. It was also shown that therapy (X-ray or cytostatics) initially causes a reduction of immunologically incompetent but later also of immunologically competent lymphocytes.

70-1424 NUCLEASES ACTIVITY IN DIFFERENT SEGMENTS OF THE HUMAN DIGESTIVE TUBE COMPARED TO THE INCIDENCE OF CARCINOMAS (HISTOCHEMICAL STUDY). (E.) Fort, L. (U. Louvain, Belgium), H. S. Taper and J. M. Brucher. Histochemie 20(2):150-158, 1969.

Alkaline and acid DNase in the stratified squamous layer of the esophageal epithelium had moderate activity (6.9% of digestive tract carcinomas are in this area; there was weak to no activity in the stomach (28% of carcinomas); intense activity in the duodenum, jejunum and ileum (0.9% of carcinomas); and a very weak nuclease activity in the colon, sigmoid and rectum (64.2% of carcinomas). Thus high nuclease activity in the digestive mucosa is inversely related to the incidence of carcinoma. Acid and alkaline RNase activity were similar to the DNase, but more in the cell cytoplasm and less in the nucleus.

70-1425 CELL RENEWAL IN THE HUMAN CERVIX UTERI. A RADIOAUTOGRAPHIC STUDY OF DNA, RNA, AND PROTEIN SYNTHESIS. (E.) Schellhas, H. F. (M. D. Anderson Hosp. Tumor Inst., Houston, Tex.). Amer. J. Obstet. Gynec. 104(5):617-632, 1969.

No overall difference was observed in the pattern and distribution of ³H-thymidine-labeled cells from biopsies of normal cervixes from untreated women and those sequentially cycled with mestranol

and chlormadionone acetate. The nuclei of the lowest layer of parabasal cells were most frequently labeled, the basal cells had a low rate of incorporation and the intermediate and superficial cells were unlabeled. Variations were not related to a specific phase in the cycle. In mild dysplasia, more of the lower cell layers were engaged in DNA synthesis, often extending into the intermediate cell layers, and basal cell layers were unidentifiable. In severe dysplasia the basal cells all but disappeared and labeled cells extended throughout the epithelial thickness, except for the uppermost layers, which showed uptake of ^3H -thymidine only in cases of carcinoma in situ.

70-1426 DEOXYRIBONUCLEIC ACID CONTENT IN BRONCHOGENIC CARCINOMA WITH SPECIAL REFERENCE TO POLYPOID CELL NUCLEI. A PRELIMINARY REPORT. (E.) Greisen, O. (U. Aarhus, Denmark). Acta Path. Microbiol. Scand. 77(2): 77-186, 1969.

Microspectrophotometric studies of biopsy material from 13 squamous-cell carcinomas, 8 adenocarcinomas and 13 oat-cell anaplastic carcinomas showed a high DNA conc. and a large dispersion of DNA content in the nuclei. However, the av. DNA conc. in the oat-cell carcinoma was slightly lower than the others and measurements indicated a small number of cells with a high DNA content. Count of the number of polyploid nuclei (per 1000 cells) in the squamous-cell and adenocarcinoma was 5.9 and 6.6, resp., but only 0.6 in the oat-cell tumor. The DNA conc. in the oat-cell polyploid nuclei was about twice the modal value, but up to 10-11 x the modal value in the other neoplasms.

70-1427 RNA SYNTHESIS IN TAPER HEPATOMA AND MOUSE-LIVER CELLS. (E.) Church, R. B. (J. Calgary, Alberta, Canada), S. W. Luther and J. McCarthy. Biochim. Biophys. Acta 190(1): 1-37, 1969.

The RNA synthesized in normal mouse liver and the taper hepatoma were compared by DNA/RNA hybridization experiments. In 8-week-old female Swiss Webster mice implanted i.p. (ascitic) or i.m. with 2×10^4 hepatoma cells, there was 100% mortality on day 12 and 18 for ascitic and i.m. tumor forms, resp. The hepatoma cells appeared to contain a more diverse selection of molecules than were present in normal liver. The tumor cell nuclei contained sequences of rapidly labeled RNA that were not transferred to the cytoplasm, although the magnitude of this intranuclear turnover appeared to be lower than in normal liver.

70-1428 IMMUNOGLOBULIN SYNTHESIS BY CULTURED MOUSE MYELOMA CELLS. (E.) Namba, Y. (Photo U. Inst. Virus Res., Japan) and M. Hanaoka. Immun. 102(6):1486-1497, 1969.

Murine myeloma cells (MOPC-31B) established in long-term culture retained the capacity to synthesize and secrete monoclonal IgG myeloma proteins for more than 20 mo. When the mechanism of synthesis was studied at cellular and subcellular levels, it was found that light (L) and heavy (H) chains were separately synthesized on different polysomes, 200 S and 280-300 S with 12 S and 22 S messenger RNA, resp. The synthesized heavy chains formed H-L complexes with free light chains, which were maintained as a large pool in the cytoplasm; $\text{H}_2\text{-L}_2$ complexes were then formed and secreted after attachment of carbohydrate.

70-1429 IMMUNOLOGICAL PROPERTIES OF LIPIDS AND THEIR RELATION TO THE TUMOR CELL. (E.) Rapport, M. M. (New York State Psychiat. Inst., N. Y.). Ann. NY Acad. Sci. 159(2):446-450, 1969.

The relationship between immunological activity and chemical structure of lipid of neoplastic tissue is presented in regard to glycosphingolipid of the plasma membrane. Rabbit anti-lipid antibodies have been obtained more readily using tumor tissue antigens, and antisera have been found to react more with total lipids of tumor, rather than normal tissue. A lactosyl ceramide (cytolipin H), similar to cerebrosides and gangliosides, has been attributed to account for much of this anti-lipid activity. Furthermore, brain tumors have been divided into 2 types - one having a high conc. of a ganglioside corresponding to monosialo cytolipin H, another with a ganglioside corresponding to disialo cytolipin H. It is suggested that in malignant transformation, the amount of complex lipid molecules in the plasma membrane decreases, with an increase in the simpler types.

70-1430 AUTOIMMUNE REACTIONS AND MALIGNANT CHANGES IN GERM-FREE NEW ZEALAND BLACK MICE. (E.) East, J. (Imperial Cancer Res. Fund, London) and M. Branca. Clin. Exp. Immun. 4(6): 621-635, 1969.

The spleens of germ-free (GF) NZB mice enlarged concomitant with Coombs positivity (7/20 mice definitely positive at 10-17 mo.). The av. spleen wt. of the 20 mice was 0.51 g as compared to an av. wt. of 1.26 g in conventional NZB mice, and 0.15 g in normal C3H/BI mice. Follicles were numerous and large, with germinal centers composed of large pyroninophilic cells, plasma blasts, plasma cells, mitotic cells and debris, present in the white pulp, and large pyroninophilic cells were also observed in the red pulp. Reticulum cell neoplasia followed and was transferred to syngeneic and BALB/c mice by i.p. inoc. of spleen cell suspensions. Evidence of lupus nephritis was seen in the kidney at 6 mo. Both the GF and the conventional mice showed signs of anemia at 6-8 mo., that of the conventional animal becoming more severe. The thymus was the

only lymphoid organ consistently larger in the GF mice.

70-1431 ALTERED CARBOHYDRATE METABOLISM AND OTHER CONSTITUTIONAL STIGMATA AND ADENOCARCINOMA OF THE UTERINE BODY. (E.) Mackay, E. V. (U. Queensland, Australia) and S. K. Khoo. *Med. J. Aust.* 1(14):724-728, 1969.

Parity distribution and hypertension, obesity and carbohydrate intolerance were studied in 43 pts. (av. age, 59.8 yr.) with endometrial carcinoma, 43 pts. (av. age, 49.6 yr.) with cervical carcinoma and 42 control pts. (av. age, 54.7 yr.) with benign gynecologic conditions, principally uterine prolapse. A significantly higher proportion of pts. with endometrial carcinoma were nulliparous (42%) and had a lower mean parity (1.7) compared with those with cervical carcinoma (12% and 4.1, resp.) and controls (17% and 2.8, resp.). No significant difference in mean blood pressures and frequency of hypertension was found, except in mean systolic pressure of pts. with endometrial and cervical carcinoma, a finding that may be related to the difference in age. The frequency of obesity among pts. with endometrial carcinoma was about twice that among controls. No significant difference in mean blood glucose values at any time interval in the oral glucose tolerance test was found between the 3 groups in 3 age divisions, except in the 1-hour level between pts. with the carcinomas in the age division over 65 yr. It is thought that aging *per se* plays a major role in the development of impaired carbohydrate metabolism and hypertension observed in pts. with endometrial carcinoma.

70-1432 GASTROINTESTINAL CANCER AND NUTRITION. (E.) Gregor, O. (Vlasska 36, Prague), R. Toman and F. Průšová. *Gut* 10(12):1031-1034, 1969.

Gastric and intestinal cancer mortality rates in 28 countries in 1962-1963 were correlated with the intake of animal protein in 1962-1963 (coefficient of correlation = -0.442 and +0.810, resp.) and in 1947-1948 (-0.530 and +0.760). The inverse relationship between the gastric and intestinal cancer mortality rates (-0.85) indicated that a large intake of animal protein was associated with low mortality from gastric cancer and a high mortality from intestinal cancer, and *vice versa*.

70-1433 MEDULLARY THYROID CARCINOMA AND PARATHYROID HYPERPLASIA IN RATS. (E.) Lindsay, S. (U. California Sch. Med., San Francisco) and C. W. Nichols. *Arch. Path. (Chicago)* 88(4):402-406, 1969.

Multiple-step sections of thyroids from 1,805 rats were reviewed and it was found that in un-

treated 2-yr.-old Long-Evans rats, the incidence of medullary carcinoma of the thyroid ranged from 23-47%, and that of parathyroid hyperplasia was 13-57%. In other rat strains (Sprague-Dawley, Fischer, Wistar, Buffalo, Osborne-Mendel), the incidence of medullary carcinoma and parathyroid hyperplasia was 19-33% and 1-30%, resp.; the incidence of both lesions in 6- and 12-mo.-old Long-Evans rats was also low. The expected and the observed incidence of both lesions occurring in the same rat were similar and thus there was no significant relationship.

70-1434 MALIGNANCY RELATED CHANGES IN THE PERIPHERAL BLOOD OF ANIMALS FOLLOWING TRANSPLANT OF TUMORS. (E.) Johnston, B. (St. Vincent's Hosp. Med. Ctr., New York, N. Y.) and J. M. Brady. *Acta Cytol. (Balt.)* 13(8):442-446, 1969.

Swiss albino male mice, 20-25 g, were inoc. i.p. with Sarcoma 37 Ascites tumor cells (20 mice) or Sarcoma 180 cells (20 mice). Daily blood smears were made and read as positive for malignancy if 50% or more large mononuclear cells had halos in their cytoplasm and if 20% or more polymorphonuclear neutrophils had fine thread-like excrescences. Slides were found to be positive 8-17 days following transplantation - after the 17th day smears from mice inj. with Sarcoma 37 were again negative and all mice inj. with Sarcoma 180 were dead.

70-1435 IMMUNOLOGICAL STUDIES ON THE MEMBRANE SYSTEMS OF CANCER CELLS. II. IMMUNOCHEMICAL SPECIFICITY OF THE MITOCHONDRIA FROM CHEMICAL CARCINOGEN-INDUCED CARCINOMA CELLS. (E.) Wakabayashi, A. (Okayama U. Med. Sch. Cancer Inst., Japan). *Acta Med. Okayama* 23(1):47-68, 1969.

A series of agar gel diffusion and immunoelectrophoresis studies with rabbit antisera against mitochondria from various rat ascites hepatoma cells (AH130, AH225A and AH66F), Yoshida sarcoma cells and the liver of normal and tumor-bearing rats is described. The antisera formed a sharp precipitin band with the various mitochondria. Tumor-bearing rat liver mitochondria (RLM) showed a common antigenicity to RLM with an additional specific antigenicity (in the α_1 and β_2 ranges) common in the tumor-bearing RLM. The 8 organ-specific mitochondrial antigens present in RLM decreased at the time of neoplastic transformation, whereas tumor mitochondria-specific mitochondrial antigenicity increased markedly. Immunization of Donryu rats with tumor cell mitochondria resulted in rejection of i.p. transplants of 2×10^7 rat ascites hepatoma cells in 27/50 rats. Adenosine triphosphatase (ATPase) activity was inhibited by 38% by rat antisera to AH130 and 29% by rabbit antisera. Rabbit antisera did not inhibit normal RLM ATPase.

AUTHOR INDEX

- Aaronson, S. A. 1293
 Abdel-Tawab, G. A. 1099
 Ackman, P. 1412
 Adenis, L. 1082,1083
 Ahlström, C. G. 1238
 Albert, R. E. 1038
 Albrecht, C. 1141
 Algard, F. T. 1130
 Ahmed, N. 1369
 Aleksandrowicz, J. 1391,1392
 Aloni, Y. 1280
 Alpert, M. E. 1374
 Altman, R. F. A. 1064
 Alvares, A. P. 1091
 Alvarez, Y. 1294
 Amaral, L. 1192
 Amaral-Mendes, J. J. 1039
 Ames, R. P. 1297
 Angervall, L. 1123
 Angulo-Hernández, O. 1362
 Aoki, T. 1262
 Araki, M. 1165
 Arcos, J. C. 1160
 Argano, S. A. P. 1163
 Argus, M. F. 1160
 Arnott, S. J. 1045
 Arseculeratne, S. N. 1109
 Asman, H. B. 1332
 Assal, N. R. 1353
 Atoynatan, T. 1276
 Auger, C. 1093
 Aungst, C. W. 1405
 Ayres, J. C. 1104,1105
- Bababunmi, E. A. 1107
 Baikie, A. G. 1015
 Bajtai, A. 1043
 Balasubramaniam, K. 1109
 Balli, L. 990
 Bandunatha, C. H. S. R. 1109
 Bapna, B. C. 1195
 Barnes, C. A. 1031,1033
 Baron, S. 1303
 Barson, A. J. 1346
 Basrur, P. K. 1177,1178
 Bassir, O. 1107,1114
 Bates, B. 1307
 Beach, D. J. 1176
 Beaudeau, G. S. 1230
 Becker, J. 1120
 Becker, K. L. 1400
 Belamaric, J. 1382
 Bendich, A. 1006
 Benedict, W. F. 1010
 Bengtsson, U. 1123
 Bennett, J. E. 1331
 Benninghoff, D. L. 1036
 Berdal, P. 1339
 Berenblum, I. 1023
 Berg, J. W. 1359
 Berry, G. 1340
 Bargarava, M. K. 1383
 Bargarava, S. K. 1383
 Bianchi, L. 1057
- Bigner, D. D. 1240
 Bingham, E. 1087
 Birbeck, M. S. C. 1103
 Birg, F. 1273
 Bischoff, F. 999
 Bishop, D. 1098
 Bixler, D. 1331
 Bjørro, K. 1128
 Black, P. H. 1287,1324
 Blackwell, R. 1101
 Blanchard, J. 1211
 Blume, R. S. 1407
 Boger, E. 1214
 Böhme, P. E. 1360
 Boiron, M. 1246
 Bonneau, H. 1273
 Borella, L. 1219,1318
 Borenfreund, E. 1006
 Borum, K. 1077
 Boschetti, E. 1229
 Brady, J. M. 1434
 Branca, M. 1430
 Breedis, C. 1327
 Bresnick, E. 1206
 Brittinger, G. 1201
 Brobst, D. F. 1268
 Brown, C. D. 1010
 Brown, G. B. 1189
 Brown, J. K. 1030
 Brown, M. 1288
 Brown, R. R. 1162
 Brucher, J. M. 1424
 Brun, J. 1044
 Bryan, G. T. 1162
 Bryant, P. J. 1194
 Bucovaz, E. T. 1184
 Bullerman, L. B. 1104
 Buncher, C. P. 1029
 Burdman, D. 1036
 Burger, M. M. 1326
 Burkhalter, A. 1205
 Burlingham, B. T. 1320
 Burns, F. J. 1038
 Burrell, R. J. W. 1386
 Buu-Hoï, N. P. 1084
- Campbell, L. V., Jr. 1354
 Campbell, T. C. 1116
 Cappelaere, P. 1080
 Caroline, N. L. 1321
 Caron, G. A. 1414
 Carr, H. W. 1155
 Carter, R. L. 1103,1216
 Case, R. A. M. 1119
 Cassingena, R. 1278
 Casto, B. C. 1308,1315
 Castor, C. W. 1418
 Cataldo, E. 1072
 Cavazzuti, F. 990
 Cazin, J. C. 1082
 Ceglowski, W. 1306
 Chakrabarty, A. 1306
 Chamorro, A. 1218
 Chaplin, M. D. 1061
- Chapman, W. H. 1171
 Chaudhry, A. P. 1075
 Chen, T. T. 1065
 Chessin, L. N. 1407
 Chesterman, F. C. 1216
 Chiga, M. 1179
 Chistiakova, Z. M. 1180
 Chlap, Z. 1272
 Chook, E. K. 1013
 Chouroulinkov, I. 1070
 Chretien, P. 1393
 Church, R. B. 1427
 Clack, J. C. 1098
 Clapp, N. K. 1147
 Claunche, B. C. 1408
 Clayson, D. B. 993
 Cocuzza, G. 1271
 Codegone, M. L. 1145
 Cohen, A. 1106
 Cohn, S. 1358
 Cole, L. J. 1081
 Condit, P. T. 1295
 Congdon, C. C. 1311
 Cook, P. 1369
 Cooper, E. H. 993,1167
 Cooper, W. C. 1292
 Correa, P. 1390
 Costarelli, A. 1271
 Cowen, D. M. 1167
 Coyle, M. 1011
 Craddock, V. M. 1144
 Craig, A. W. 1147
 Craig, R. L. 1066
 Crawford, M. A. 1368
 Crist, S. B. 1168
 Cuenca, C. R. 1400
 Cuello, C. 1390
- Dabbert, A. F. 1370
 Dais, C. F. 1184
 Dalquen, P. 1370
 Dalton-Tucker, M. F. 1281,1282
 Dao, T. L. 1069
 Darnell, J. E. 1283
 Da Silva, D. J. 1064
 Datta, S. P. 1068
 Davidson, A. 1071
 Davidson, C. S. 1374
 Davies, R. F. 1096,1097
 Davis, W. C. 1040
 Day, E. D. 1240
 De Albertis, P. 994
 Debski, T. 1391
 Deckert, M. 1211
 DeCosse, J. J. 1197
 Defendi, V. 1323
 Deinhardt, F. 1249,1312
 de Lustig, E. S. 1056
 DeNyse, D. 1408
 de Serres, F. J. 1158
 De Silva, L. M. 1109
 Dewhurst, F. 1092
 d'Hooghe, M. 1080
 Diamandopoulos, G. T. 1281,1282

- Dicke, T. E. 1102
 Dienst, H. 1161
 Dikow, A. L. 1148
 Di Luzio, N. R. 1416
 Di Stefano, H. S. 1012
 Doell, R. G. 1203
 Doerfler, W. 1320
 Donschewa-Stratewa, N. 1378
 Dougherty, R. M. 1012
 Driessens, J. 1080,1082,1083
 Drolette, M. 1335
 Drożdżewska, Z. 1373
 Druckrey, H. 1005,1191,1193
 Dubbs, D. R. 1278,1279
 Dubrow, H. 1387
 Duke, G. A. 1196
 Dulac, G. C. 1268
 Duncan, R. M. 1085
 Dungworth, D. L. 1034
 Dunn, J. E., Jr. 1337
 Duque, E. 1390
 Durst, A. 1076
- East, J. 1430
 Easton, J. M. 1267
 Ebbesen, P. 1232
 El-Shafei, A. K. 1099
 El-Zoghby, S. M. 1099
 Emafo, P. O. 1114
 Emanoil-Ravicovitch, R. 1246
 Epstein, L. I. 1331
 Erdős, Z. 1348
 Evans, A. S. 1256
 Everett, M. A. 1295
 Ezdinli, E. Z. 1405
- Fabia, J. 1335
 Fabrikant, J. I. 1420
 Fadda, G. 1234
 Fahmy, M. J. 1182
 Fahmy, O. G. 1182
 Falk, H. L. 1087,1095
 Fechner, R. E. 1126
 Feinleib, M. 1388
 Fenton, A. N. 1358
 Fernandes, G. 1190
 Fey, F. 1223,1224
 Fialkow, P. J. 1394
 Fickling, B. W. 1419
 Filipiak, B. 1111
 Finlayson, N. D. C. 1045
 Fischer, H. 1286
 Fisher, E. R. 1233
 Flehinger, B. J. 1387
 Fleissner, E. 1313
 Fogh, J. 1300,1317
 Foley, G. E. 1172
 Foley, W. A. 1081
 Fort, L. 1424
 Fouts, J. R. 1090
 Fox, H. 1357
 Fox, R. R. 1231
 Fraumeni, J. F., Jr. 1334
 Frei, J. V. 1185
- Friberg, S., Jr. 1248
 Friedman, H. 1306
 Fudenberg, H. H. 1040
 Fukui, K. 1259,1262
 Furst, A. 996
 Furuno, A. 1289
- Gadomska, H. 1373
 Gaffney, E. V. 1300,1317
 Gallagher, T. F. 1412
 Garbut, A. 1091
 Garcia, H. 1187
 Garret, M. 1036
 Garrison, R. J. 1388
 Gavankar, M. H. 1253
 Gavitt, F. 1312
 Gaylor, J. L. 1060
 Gentil, A. 1070
 Geraldies, A. 1270
 Ghali, F. H. 1366
 Ghose, T. 1068
 Giblett, E. R. 1394
 Gilbertsen, V. A. 1344
 Gilman, J. P. W. 1177,1178
 Giorgi, R. 1113
 Gisin, S. 1235
 Glade, P. R. 1407
 Glass, A. G. 1345
 Glick, J. L. 1257
 Glover, E. L. 1050
 Godbole, V. K. 1364
 Goldenberg, D. M. 1233
 Goldman, M. 1034
 Goldner, H. 1316
 Good, R. A. 1198
 Gordon, D. E. 1269
 Górski, T. 1021
 Gothoskar, S. V. 1190
 Gotoh, S. 1143
 Grace, J. T., Jr. 1227
 Graffe, L. H. 1285
 Grahm, B. 1243
 Gralnick, H. R. 1407
 Green, M. 1260
 Gregor, O. 1432
 Greisen, O. 1426
 Grieshaber, E. 1250,1251, 1298
 Guillon, J.-C. 1070
 Gurda, M. 1392,1397
 Gurtoo, H. L. 1116
 Gusberg, S. B. 1136
 Guttman, P. H. 1040
- Haase, A. T. 1407
 Hacker, B. 1319
 Hadjiolov, D. C. 1148
 Haenszel, W. 1338
 Hairstone, M. A. 1292
 Hakama, M. 1380
 Hamilton, T. 1041
 Hammond, E. C. 1355
 Hanada, M. 1139
 Hanaki, A. 1137
- Hanaoka, M. 1428
 Hanks, C. T. 1075
 Hansen, I. L. 1368
 Harley, E. H. 1106
 Harlow, R. A. 1037
 Haro, R. T. 996
 Harris, C. 1210
 Harris, C. C. 1179
 Hartman, P. A. 1104
 Hartwell, J. L. 1022
 Hartwich, G. 1120
 Haughton, G. 1009,1209
 Hausknecht, R. U. 1136
 Hayry, P. 1323
 Hayward, A. F. 1419
 Hebert, G. J. 1177
 Heidelberger, C. 1065
 Heimbach, R. D. 1038
 Heine, K.-M. 1423
 Hellman, L. 1412
 Hellriegel, K. P. 1406
 Henderson, E. S. 1225
 Herbertson, R. M. 1352
 Herrold, K. M. 1154
 Herron, J. 1381
 Hiasa, Y. 1156
 Hicks, C. 1192
 Hienz, H. A. 1201
 Higashi, K. 1143
 Hiltz, J. E. 1042
 Hino, S. 1242
 Hinz, I. 1370
 Hirai, M. 1052
 Hiramatsu, T. 1156
 Hoch-Ligeti, C. 1160
 Hodenberg, A. v. 1174,1193
 Hodes, M. E. 1035
 Hodes, R. J. 1248
 Hoffmann, M. 1149
 Holland, J. F. 1330
 Holmberg, E. A. D. 1032
 Holmes, H. L. 1031
 Homburger, F. 1214
 Honda, Y. 1006
 Hopewell, J. W. 1094
 Hopkin, I. D. 1037
 Hosoi, H. 1151
 Howland, R. D. 1205
 Hruban, Z. 1341
 Hsiung, G. D. 1276,1328
 Huebner, R. J. 1220,1221,1222, 1235,1303,1305,1314
 Hulse, E. V. 1028
 Humphrey, L. H. 1417
 Humphrey, L. J. 1063
 Hunter, L. 1063
 Hutt, M. S. R. 1374
- Iijima, S. 1029
 Ilbery, P. L. T. 1031,1033
 Imagawa, D. T. 1309
 Imahori, S. 1304
 Imoto, T. 1156
 Ionescu-Homoriceanu, S. 1285
 Ishikawa, M. 1156

- Ito, N. 1156
 Itoh, K. 1169
 Ivankovic, S. 1005, 1191, 1193
 Iype, P. T. 1065
- Jabłoński, L. 1284
 Jacob, A. 1138
 James, H. L. 1184
 Janicki, J. 1111
 Janicki, M. 1392
 Jänisch, W. 1153
 Janss, D. H. 1212
 Jaszcz, W. 1272
 Jefcoate, C. R. E. 1060
 Jenson, C. B. 1351
 Jerkofsky, M. A. 1329
 Jewell, W. R. 1063
 Johnston, B. 1434
 Jones, B. 1336
 Jones, H. W., Jr. 1395
 Jones, O. W. 1168
 Jonsson, N. 1244
 Juberg, R. C. 1336
 Juhasz, J. 1043
 Juźwiak, J. 1118
- Kajima, M. 1301
 Kalima, T. B. 1379
 Kanazawa, K. 1103
 Kanemasa, Y. 1264
 Kantemir, I. 1078
 Kaplow, L. S. 1328
 Karwacka, H. 1284
 Karwowski, A. 1350
 Kato, S. 1258
 Katz, J. L. 1412
 Kaul, B. L. 1399
 Kawazoe, Y. 1165
 Kawecka-Jaszcz, K. 1272
 Kawecki, K. 1132
 Keast, D. 1199, 1200
 Kelada, F. S. 1099
 Kelisky, R. P. 1387
 Keller, A. Z. 1384
 Keller, H.-P. 1261
 Kelley, T. F. 1170
 Kerzner, M. S. 1408
 Key, C. R. 1029
 Khou, S. K. 1431
 Khundanova, L. L. 1180
 Kibuchi, Y. 1046
 Kim, U. 1405
 Kimoto, K. 1140
 Kimura, S. 1259, 1262
 King, A. M. Q. 1112
 King, V. P. 1229
 Kirkland, J. A. 1396
 Kirkman, H. 1130
 Kirkpatrick, D. 1330
 Kirkpatrick, R. 1330
 Kit, S. 1278, 1279, 1288
 Kitchin, D. A. 1092
 Kjaas, D. J. 1377
 Kiehu, P. 1191
- Klug, H. 991
 Knutsen, T. 1393
 Kofman, J. 1044
 Kołodziejska, H. 1375
 Kolompár, G. 1275
 Komitowski, D. 1134
 König, E. 1201
 Konishi, Y. 1156
 Koprowski, H. 1277
 Korosteleva, T. A. 1180
 Korzeniowska, A. 1350
 Koss, L. G. 1387
 Koszarowski, T. 1373
 Kotin, P. 1095
 Kovács, E. 1275
 Kozenitzky, I. L. 1409
 Krarup, T. 1074
 Krasnow, S. 1343
 Krause, W. 1365
 Krawczyk, M. 1350
 Kraybill, H. F. 1014
 Kreider, J. W. 1327
 Krishnamurthi, S. 1363
 Kroh, H. 1051
 Krüger, F. W. 1146
 Kung, T. 1307
 Kuntzman, R. 1062, 1091, 1207
 Kurimura, T. 1278
 Kurland, L. T. 1349
 Kwittken, J. 1401
 Kyle, R. A. 1349
- Laird, C. W. 1231
 Lamberson, H. V. 1252
 Lane, W. T. 1221, 1314
 Laqueur, G. L. 995
 Lasfargues, E. Y. 1254
 Lasfargues, J. C. 1254
 Lasne, C. 1070
 Lausch, R. N. 1322
 Lawler, S. D. 1398
 Layne, S. 1322
 Leader, R. W. 1025
 Leavell, U. W., Jr. 1417
 Lee, C. W. 1276
 Lee, K. P. 1269
 Lee, S. S. 1108
 Lehtonen, M. 1380
 Lemon, H. M. 1333
 Lesko, S. A., Jr. 1088
 Lespagnol, A. 1082
 Leuchtenberger, C. 1211
 Leuchtenberger, R. 1211
 Levi, P. E. 1167
 Levij, I. S. 1076, 1164
 Levin, W. 1062, 1207
 Levy, J. A. 1247
 Li, C. P. 1310
 Li, E. P. 1225
 Li, F. P. 1334
 Liban, E. 1409
 Libby, P. R. 1069
 Lijinsky, W. 1187
 Lillard, H. S. 1105
 Lincoln, P. 1063
- Lind, K. 1232
 Lindberg, L. G. 1236, 1237, 1238
 Lindberg, U. 1283
 Lindeman, R. D. 1353
 Lindsay, S. 1433
 Lingeman, C. H. 1016
 Lisker, R. 1394
 Liu, G. X. 1108
 Lopes, C. R. N. 1064
 Lopez, A. 1368
 Loveless, J. D. 1300
 Lowe, C. R. 1385
 Lowry, J. 1213
 Lucas, R. B. 1419
 Luschnitz, E. 1261
 Luther, S. W. 1427
 Lynch, F. W. 1355
 Lyons, M. 1307
- Maag, T. 1319
 Mackay, E. V. 1431
 MacMahon, B. 1356, 1385
 Magee, P. N. 998
 Magnin, F. 1044
 Mahaley, M. S., Jr. 1240
 Main, J. H. P. 1274
 Major, I. R. 1188
 Malendowicz, L. 1111
 Mallet, L. 1093
 Mallin, H. V. 1158
 Malmgren, R. A. 1267
 Mandel, L. R. 1319
 Mandel, M. A. 1197
 Mandelstam, P. 1213
 Mannering, G. J. 1061
 Manocha, S. L. 1054
 Mantel, N. 1345
 Marczyńska, B. 1312
 Mariani, T. 1302
 Martino, E. C. 1310
 Masubuchi, Y. 1052
 Masuji, H. 1166
 Matos, E. L. 1056
 Matsuhisa, T. 1143
 Matsumoto, S. 1191
 Matte, R. 1402
 Maurer, B. A. 1257
 McCarthy, B. J. 1427
 McCollum, R. W. 1256
 McGlashan, N. D. 1122
 McIntire, K. R. 1175
 McKelvie, D. H. 1034
 McNeill, J. R. 1030
 Medrás, K. 1131
 Meeker, W. R., Jr. 1227
 Meezan, E. 1287, 1324
 Meier, H. 1231, 1305
 Melamed, M. R. 1387
 Melchionne, S. 1008
 Meranze, D. R. 1316
 Merigan, T. C. 1040
 Merkow, L. P. 1265
 Meyer, G. 1273
 Meyer, K. K. 1125
 Mieler, W. 1026

- Mietkiewski, K. 1111
 Miller, E. 1101
 Miller, E. C. 997
 Miller, J. A. 997
 Minowada, J. 1257
 Mirand, E. A. 1227
 Miroff, G. 1252
 Miura, M. 1058
 Mody, J. K. 1253
 Moloney, W. C. 1229
 Monjour, L. 1113
 Moon, R. C. 1212
 Moore, D. H. 1254
 Morgan, J. M. 1135
 Morris, H. P. 1341
 Morrison, J. C. 1184
 Mosse, H. 1206
 Moutaffian, J.-J. 1415
 Mukai, F. 1183
 Munk, K. 1286
 Munroe, I. 1307
 Myers, D. D. 1231,1305
 Myhre, E. 1128
 Myrden, J. A. 1042
- Nachtigal, M. 1285
 Nagao, M. 1151
 Nagata, C. 1165
 Nagel, G. 1330
 Naito, M. 1258
 Nakai, M. 1309
 Nakajima, K. 1278
 Nakao, T. 1052
 Namba, M. 1166
 Namba, Y. 1428
 Nash, D. R. 1009
 Nath, A. 1195
 Nau, C. A. 1124
 Naylor, B. 1102,1418
 Neiders, M. E. 1075
 Neubauer, S. 1303
 Newberne, P. M. 1110
 Newell, G. R. 1342
 Ng, A. B. P. 1361
 Niaussat, P. 1093
 Nicholls, E. M. 1413
 Nichols, C. W. 1433
 Nichols, W. W. 1002
 Nicholson, B. H. 1112
 Niederman, J. C. 1256
 Nishimura, R. 1196
 Nobrega, F. T. 1349
 Nordeck, E. 1360
 Nordquist, R. E. 1295
 Nosek, H. 1375
 Nowell, P. C. 1003
- Obara, Y. 1402
 O'Brien, R. L. 1066
 Odaka, T. 1217
 Odom, G. L. 1240
 Oehlert, W. 1057
 Ohmori, M. 1263,1264
 Oka, H. 1029
- Okajima, E. 1156
 Okamoto, T. 1266
 Okano, T. 1181
 Olmer, J. 1415
 Olson, C. 1269
 Olson, R. L. 1295
 Oluwasanmi, J. O. 1371
 Ondok, J. 1376
 O'Neill, C. H. 1325
 Ono, K. 1258
 Opler, S. R. 1226
 Osunkoya, B. O. 1371
 Owen, J. 1071
- Palestro, G. 1145
 Pardo, M. 1265
 Parham, J. C. 1189
 Parkman, R. 1247
 Parr, B. 1215
 Pasqualini, C. D. 1032,1228
 Paul, B. 1010
 Pearson, G. R. 1248
 Pearson, J. G. 1045
 Pedio, G. 1250,1251,1298
 Pellin, J. C. 1401
 Peltokallio, P. 1379
 Peters, J. A. 1022
 Peto, R. 1098
 Petrow, Z. D. 1423
 Pfeiffer, R. A. 1406
 Phillips, M. E. 1046
 Pierce, E. R. 1332
 Pierce, G. B. 1421
 Pilch, Y. H. 1059
 Pillsbury, N. 1254
 Pintado, T. 1294
 Pipkin, G. E. 1100,1196
 Pisano, J. C. 1416
 Playforth, H. 1417
 Pohnke, B. 1047
 Pollard, M. 1296,1301
 Polliack, A. 1076,1164
 Porter, I. H. 1010
 Potter, V. R. 1142
 Pound, A. W. 1186
 Pratt, P. T. 1333
 Prescott, B. 1310
 Preussmann, R. 1005,1174,
 1191,1193
 Princler, G. L. 1175
 Proffitt, M. R. 1311
 Průšová, F. 1432
- Rabasa, S. L. 1032,1228
 Rabin, B. R. 1115
 Rabin, H. 1239
 Rabson, A. S. 1267
 Raick, A. N. 1204
 Ramming, K. P. 1059
 Ramos, L. 1317
 Ranadive, K. J. 1190,1253
 Rapoza, N. P. 1265
 Rapp, F. 1322,1329
 Rapport, M. M. 1429
- Reagan, J. W. 1361
 Rechcigl, M., Jr. 1341
 Reedy, J. K. 1179
 Rees, E. D. 1213
 Rees, K. R. 1106
 Reeves, J. A. 1408
 Refsum, S. B. 1339
 Reichel, G. 1117
 Reid, E. 1173
 Reuber, M. D. 1050
 Rhim, J. S. 1220,1221,1222,
 1314
 Rice, J. M. 1152
 Rickers, H. J. 1406
 Rickert, D. E. 1090
 Rigby, P. G. 1333
 Ritchie, A. C. 1204
 Robbins, M. 1011
 Robbins, P. W. 1287,1324
 Robertson, H. T. 1324
 Robl, M. G. 1269
 Roe, F. J. C. 1098,1103
 Rohrbach, R. 1067
 Rose, E. F. 1121
 Rosengren, E. 1243
 Rosenkranz, H. S. 1150,1155
 Rosenkranz, S. 1150
 Rosenlof, R. C. 1333
 Rossano, R. W. 1358
 Rothwax, Y. 1412
 Rowson, K. E. K. 1215,1216
 Royall, H. J. 1018
 Rózewicki, S. 1047
 Rubin, R. 1297
 Rücker, U. 1146
 Ruszkowska, E. 1350
 Rüttner, J. R. 1250,1251,1298
 Rybaczek, B. 1350
- Saal, F. 1228
 Sachar, E. J. 1412
 Sachs, L. 1280
 Saffiotti, U. 1089,1187
 Sagara, Y. 1262
 Sahnazarov, N. 1285
 Saito, M. 1172
 Sakamoto, Y. 1143
 Salaman, M. H. 1216
 Salas-Martínez, M. 1362
 Salber, E. J. 1356
 Salky, N. K. 1416
 Sampson, R. J. 1029
 Sandberg, A. A. 1405
 Sang, J. H. 1194
 Sanger, R. 1398
 Sarma, P. S. 1303
 Sasaki, M. 1402
 Sato, J. 1166
 Saxén, E. 1380
 Schachtschabel, D. O. 1172
 Schellhas, H. F. 1425
 Schiffer, Z. 1391,1392
 Schilling, G. 1091
 Schindler, R. 1007
 Schlegel, J. U. 1100,1196

- Schmidt, R. M. 1150
 Schneider, J. 1153
 Schoental, R. 1004
 Schottenfeld, D. 1359
 Schreiber, D. 1153
 Schütz, C. 1406
 Schwanitz, G. 1120
 Scully, R. E. 1403
 Seidman, H. 1355
 Seiler, R. 1406
 Semple, J. C. 1404
 Sen, D. K. 1357
 Shah, H. H. 1364
 Shanta, V. 1363
 Sharma, A. K. 1053
 Sharon, N. 1296
 Shcherbak, N. P. 1086
 Shearman, D. J. C. 1045
 Sherry, J. B. 1127
 Shima, S. 1052
 Shimkin, M. B. 1019
 Shiu, G. 1303
 Shklar, G. 1072,1073
 Shoeman, D. W. 1061
 Shubik, P. 1022
 Shultz, G. N. 1100
 Sieracki, J. C. 1233
 Sigmon, E. 1209
 Sil, R. 1048
 Simpson, J. S. 1346
 Sims, P. 1049
 Singh, S. M. 1195
 Sirsat, S. M. 1055
 Sladen, W. J. L. 1239
 Slifkin, M. 1265
 Smart, C. R. 1351,1352
 Smith, C. W. 1124
 Smith, R. D. 1202
 Snider, T. W. 1142
 Snyder, A. L. 1225
 Snyder, S. P. 1249
 Sokal, J. E. 1405
 Soll, C. 1365
 Southam, C. M. 1058
 Spain, D. M. 1163
 Spatz, M. 1017
 Spiers, A. S. D. 1015
 Stanley, M. A. 1396
 Stanley, N. F. 1199
 Stanton, M. F. 1101
 Stantron, R. 1066
 St-Arneault, G. 1330
 Steele, W. J. 1208
 Steigrad, S. J. 1367
 Steinglass, M. 1006
 Steplewski, Z. 1277
 Stevens, P. J. 1037
 Stewart, S. E. 1255
 Stjernvall, L. 1079,1422
 Stobbe, H. 1423
 Stocks, P. 1389
 Trauss, B. 1011
 Trzelecki, E. 1105
 Tohr, G. 1161
 Tutman, O. 1198
 Uarez, H. G. 1291
 Ubrahmany, L. 1256
 Sugimura, T. 1151
 Sugiura, K. 1189
 Sunderman, F. W., Jr. 1176
 Sung, S. S. 1084
 Sutton, C. H. 1297
 Svoboda, D. J. 1179
 Svoboda, V. 1376
 Switzer, J. W. 1034
 Sykes, A. K. 1178
 Synowiedzka, E. 1350
 Szeder, M. 1348
 Szöke, L. 1348
 Tabarés, E. 1294
 Tabata, M. 1137
 Taga, N. 1137
 Takeuchi, M. 1241,1242
 Talbert, J. R. 1127
 Talukder, G. 1053
 Tanabe, S. 1258
 Taper, H. S. 1424
 Tapp, E. 1133
 Tauchnitz, C. 1261
 Taylor, A. T. 1168
 Tedeschi, F. 1234
 Teller, M. N. 1161,1189
 Tennekoon, G. E. 1109
 Tenney, V. A. 1411
 Tevethia, S. S. 1322
 Theilen, G. H. 1249
 Theuring, F. 1372
 Thomas, C. G., Jr. 1071
 Ting, R. C. 1220,1247
 Tipnis, U. V. 1055
 Tobin, M. S. 1163
 Todaro, G. J. 1225,1293
 Toman, R. 1432
 Tominaga, T. 1069
 Toprani, H. T. 1364
 Török, A. 1348
 Torten, J. 1280
 Toury, J. 1113
 Toya, R. E., Sr. 1147
 Treger, A. 1214
 Trentin, J. J. 1308,1315
 Trichopoulos, D. 1356
 Troll, W. 1183
 Tseng, P.-Y. 1395
 Ts'o, P. O. P. 1088
 Tsuji, K. 1181
 Tsunooka, H. 1347
 Tsuru, K. 1290
 Turano, A. 1234
 Turbiner, S. 1072,1073
 Turner, H. C. 1314
 Turusov, V. S. 1020
 Uchiyama, I. 1137
 Uehleke, H. 1000
 Ulmer, W. T. 1117
 Umans, R. S. 1088
 Urata, Y. 1052
 Urbanowicz, M. 1111
 Valladares, Y. 1294
 van der Noordaa, J. 1282
 Van Duuren, B. L. 1001,1008
 Van Griensven, L. 1246
 Van Hoosier, G. L., Jr. 1308, 1315
 Vass, W. 1220
 Vernole, B. 990
 Vernon, M. L. 1221
 Vigier, P. 1245
 Vitak, M. J. 1420
 Vitsky, B. 1359
 Vizoso, A. D. 1299
 Vlaeminck, M. N. 1083
 Waggoner, D. E. 1342
 Wagner, J. 1209
 Wagner, J. C. 1340
 Wakabayashi, A. 1435
 Wakabayashi, T. 1027
 Warzok, R. 1153
 Watne, A. L. 1354
 Watson, K. F. 1230
 Wechsler, W. 1191
 Wedderburn, N. 1216
 Wei, R. D. 1108
 Weiner, H. 1412
 Weir, J. M. 1337
 Wender, S. H. 1124
 Werner, U. 1117
 Werthamer, S. 1192
 Whang-Peng, J. 1393
 Wheelock, E. F. 1321
 Whitehead, J. K. 1097
 Whittle, E. D. 1157
 Wiessler, M. 1146
 Wijesundera, S. 1109
 Williams, D. J. 1115
 Williams, G. 1110
 Winocour, E. 1280
 Wisseman, C. L., III 1420
 Wivel, N. 1220
 Wold, J. W. 1208
 Wolfe, G. 1249
 Wolff, S. M. 1407
 Wood, J. L. 1184
 Wu, H. 1324
 Wu, H. C. 1287
 Wuest, H. 1058
 Wyatt, A. P. 1410
 Yamamoto, T. 1027,1241,1242
 Yamane, Y. 1137
 Ydrach, A. A. 1129
 Yip, L. C. 1035
 Yokoshima, T. 1151
 Yoshida, N. 1259,1262
 Yoshida, O. 1162
 Yoshiike, K. 1289
 Yunis, E. J. 1198
 Zavala, C. 1394
 Zawirska, B. 1131
 Zetterlund, C. G. 1123
 Zeve, V. 1293
 Zijlstra, V. L. J. 1024
 Zilliken, F. 1172
 Zimmerman, H. M. 992,1297
 Zorini, A. O. 1159
 Zsigmond, M. 1123
 Zülch, K. J. 1191

SUBJECT INDEX

ABSORPTION, INTESTINAL

polycyclic aromatic hydrocarbons, mechanism,
animal: 1213

2-ACETYLAMINOFLUORENE (See N-2-Fluorenylacetamide)

ACRIDINE

epidermal hyperplasia, mouse skin: 1188

ADJUVANTS, Freund's, mouse plasmacytoma, leukemia
virus-like particles: 1250,1251

ADRENAL

necrosis, dimethylbenzanthracene-induced,
mechanism, rat: 1210

ADRENAL NEOPLASMS

lead acetate induction, rat: 1131

AFLATOXIN(S)

bioassay method, amphibian larvae or chick
embryo: 1109

content, meats: 1104,1105

effect on blood coagulation, rat: 1107

liver tumors, methylation of transfer or
ribosomal RNA, rat: 1144

metabolism, rat, monkey or human: 1113

AFLATOXIN B-1

effect on

DNA, RNA and protein, tumor cells: 1106

microsomal benzpyrene hydroxylase, rat
liver: 1116

polynucleotides and RNA polymerase, cell-
free system: 1112

liver tumors, rat: 1111

effect of diethylstilbestrol: 1110

metabolism, mammalian liver microsomes:

1114,1115

uptake and liver toxicity, skin painting, rat:
1108

AGE FACTORS

breast cancer, international: 1388

leukemia risk, review: 1013

skin cancer, Germany (Giessen): 1365

AIR POLLUTION

benzpyrene, analytical method: 1085

ALCOHOLIC BEVERAGES

analysis, high-esophagus cancer regions,
central Africa (Zambia and Malawi): 1122

ALCOHOLISM

liver cirrhosis, malignant transformation:
1415

AMINES AND AMIDES, AROMATIC

activation to active carcinogens, mechanism,
review: 997

environmental and occupational exposure,
bladder cancer: 1119

toxicity, mechanism, review: 1000

ANTHRANILIC ACID, 3-HYDROXY-

effect on urinary cinnabarinic acid formation,
bladder cancer: 1196

excretion, bladder cancer: 1195

dietary factors, Africa (Uganda): 1368

ANTITUMOR AGENTS

busulfan, effect on WBC chromosomes, poly-
cythemia vera: 1031

liver extract from clam (*Mercenaria mercenaria*),
effect on adenovirus-12 tumor, hamster:
1310

mitomycin C, effect on liver phospholipids,
dimethylaminoazobenzene hepatoma, rat: 1139

ANTITUMOR AGENTS, (Contd.)

streptozotocin, mechanism of action, bacteria
and tumor cells: 1155

vinblastine, effect on dimethylbenzanthracene
skin tumors, resistant mouse strain: 1079

ARSENIC

occupational exposure, chronic toxicity,
Poland (Zloty Stok): 1118

ASBESTOS

asbestos bodies, prevalence, Michigan (Detroit
and Lower Peninsula): 1102

environmental exposure, review: 1018

lung tumors or mesothelioma, rat: 1101,1340

migration from s.c. inj. sites, mouse: 1103

occupational exposure, pleural mesothelioma,
West Germany (Hamburg): 1370

AZOBENZENE, N-BENZOYLOXY-N-ETHYL-4-AMINO-
mutagenesis, *Drosophila*: 1182

AZOBENZENE, 4-DIMETHYLAMINO-

effect on WBC phagocytic activity, rat: 1180
liver tumors (rat)

effect on copper salt: 1137

establishment of new ascites hepatomas:
1140

pentose phosphate metabolism: 1138

riboflavin effect on liver phospholipids:
1139

AZOBENZENE, 3'-METHYL-4-DIMETHYLAMINO-

effect on WBC phagocytic activity, rat: 1180
liver tumors (rat)

nuclear fractionation by ploidy: 1141

nucleolar RNA composition: 1143

thymidine triphosphate metabolism: 1142

AZOBENZENE, 4'-METHYL-4-DIMETHYLAMINO-

liver tumors, nucleolar RNA composition, rat:
1143

AZOTOLUENE, o-AMINO-

liver tumors, morphology of premalignant
tumors, mouse: 1169

AZO COMPOUNDS, ALIPHATIC

structure-activity relationship, rat: 1193

1,2-BENZANTHRACENE

epidermal hyperplasia, mouse skin: 1188

skin tumors, cocarcinogen effects on threshold
response, mouse: 1087

BENZANTHRACENE, 7-BROMOMETHYL-12-METHYL-
mutagenesis, *Drosophila*: 1182

BENZANTHRACENE, 1,2,3,4-DI-

epidermal hyperplasia, mouse skin: 1188

BENZANTHRACENE, 1,2,5,6-DI-

epidermal hyperplasia, mouse skin: 1188

BENZANTHRACENE, 1,2,7,8-DI-

epidermal hyperplasia, mouse skin: 1188

BENZANTHRACENE, 7,12-DIMETHYL-

adrenal necrosis, mechanism, rat: 1210

cervix tumors, effect of contraceptives,
mouse: 1128

cheek pouch tumors (hamster)

effect of orchiectomy: 1076

pathology: 1075

distribution, mammary gland, effect of
oophorectomy or hypophysectomy, rat: 1212

BENZANTHRACENE, 7,12-DIMETHYL- (Contd.)

- effect on
 - DNA, rat mammary gland, sex difference: 1069
 - regenerating mouse liver: 1204
- epidermal hyperplasia, mouse skin: 1188
- intestinal absorption, animal: 1213
- mammary tumors
 - effect of crowding, rat: 1070
 - malatonin and environmental light, rat: 1041
 - surgical trauma (mastectomy), rat: 1071
 - virus-positive, low-spontaneous mammary tumor mouse strain: 1253
- mutagenesis, Drosophila: 1182
- ovarian tumors, mouse: 1074
- + radiation, lung tumors, mouse: 1039
- salivary gland tumors
 - effect of cold stress, rat: 1072
 - strain difference, rat: 1073
- skin tumors (mouse): 1078
 - DOPA oxidase-positive melanocytes: 1067
 - effect of vinblastine or dimethyl sulfoxide, skin tumor-resistant strain: 1079
 - sex difference, effect of thymectomy: 1077
- thymoma, host immunity, effect of thymectomy, mouse: 1198

ENZANTHRENE DERIVATIVES

- cysteine conjugates, effect on aminoacyl-RNA synthetase, cell-free system: 1184

metabolism, effect of methylcholanthrene, rat liver microsomes: 1049

- skin tumors, structure-activity relationship, mouse: 1187

ENZENE

- occupational exposure, leukemia, chromosomal abnormalities: 1120

ENZO(rst)PENTAPHENE (See Benzpyrene, 3,4,9,10-di-4-BENZPYRENE

- analysis, method, air pollution: 1085
- attempted s.c. tumor induction, cattle: 1068
- biliary excretion, effect of pesticide synergists, rat: 1095
- biosynthesis, bacteria, effect of culture medium constituents: 1093
- brain tumors, effect of orchietomy, rat: 1094
- cervical atypia, radiation effects, mouse: 1036
- DNA complex, properties: 1066,1088
- intestinal absorption, mechanism, animal: 1213
- lung or stomach tumors, effect of vitamin A, hamster: 1089
- mechanism of action, theoretical model: 1084
- metabolism, rat liver microsomes: 1090, 1091, 1116
- skin tumors (mouse): 1078
 - cocarcinogen effects on threshold response: 1087
- soil and vegetation pollution, petroleum processing plant, USSR: 1086
- solid tumors, chromosomes, rat: 1053
- transplantable mouse sarcoma, effect of guinea pig RNA: 1059

4-BENZPYRENE, 3,4,9,10-DI-

- distribution, mouse: 1170

BENZPYRENE, 3,4,9,10-DI- (Contd.)

- s.c. tumors, prevention by essential oils, mouse: 1214

BENZPYRENE DERIVATIVES

- metabolism, effect of methyocholanthrene, rat liver microsomes: 1049
- 6-substituted, effect on zoxazolamine paralysis time, rat: 1092

BERYLLIUM

- bone sarcomas, rabbit: 1133,1134

BILIARY TRACT NEOPLASMS

- epidemiology
 - Germany (Göttingen-Weende): 1360
 - sex ratio, England/Wales and western Europe: 1389

BLADDER

- cell growth rate, effect of ethylsulfonyl-naphthalene-1-sulfonamide, mouse: 1167

BLADDER CARCINOGENESIS

- animal, review: 993
- aromatic amines, environmental and occupational exposure: 1119
- ethylsulfonylnaphthalene-1-sulfonamide, mouse: 993
- fluorenylacetaamide, effect of bladder parasite, rat: 1171
- 4-nitrosamino-4-n-butyl-n-butanol, rat: 1156

BLADDER NEOPLASMS

- cinnabaric acid excretion, human: 1196
- epidemiology, smoking, U.S.: 1337
- excretion of carcinogenic tryptophan metabolites, human: 1195,1196
- phenacetin abuse, Sweden: 1123
- recurrence rate, tryptophan metabolism, human: 1162
- urinary chemiluminescence, smokers: 1100

BLOOD

- coagulation, effect of aflatoxin, rat: 1107

BLOOD GROUPS

- Gc, leukemia, Poland: 1397
- Xg type, Ph¹-positive or -negative chronic myeloid leukemia: 1394,1398

BONE MARROW

- cells, site of Friend virus susceptibility locus, mouse: 1217

BONE MARROW DISEASES

- myelofibrosis with myeloid metaplasia, saponin induction, rabbit: 1163

BONE NEOPLASMS

- atomic radiation exposure, Hiroshima/Nagasaki: 1027
- osteogenic sarcoma
 - beryllium induction, rabbit: 1133,1134
 - familial: 1331
- radiation, induction, rabbit: 1028
- sarcoma at site of injury, Paget's disease: 1404

BRAIN NEOPLASMS

- epidemiology
 - children, Hungary: 1348
 - review: 992
- induction
 - benzpyrene, effect of orchietomy, rat: 1094
 - methods, animal, review: 992
 - methylcholanthrene, mouse: 1048,1051

BRAIN NEOPLASMS, (Contd.)

- virus-like particles, mouse: 1297
- methylnitrosourea, dog: 1153
- nitroso compounds, transplacental, rat: 1191
- Rous sarcoma virus, dog: 1240
- meningeal fibroma and brain tumors, induction, bovine papilloma virus, calf: 1268
- tumor cell lipids, structure and antigenic activity: 1429

BREAST NEOPLASMS (See Mammary neoplasms, human)

n-BUTANOL, 4-NITROSAMINO-4-n-BUTYL-

- bladder tumors, rat: 1156

CADMIUM

- serum and tissues, lung and other cancer, human: 1135

CARBAMATES

- butyl or isoamyl carbamate, effect on urethan lung tumors, mouse: 1082

CARBOHYDRATES

- intolerance, endometrial cancer: 1357,1431

CARCINOGENESIS, CHEMICAL

- aliphatic azo compounds and triazenes structure-activity relationship, rat: 1193
- aromatic amines and amides, mechanism, review: 997
- epoxides, lactones and halo-ethers, mechanism, animal, review: 1001
- inhibition, mechanism, review: 1008
- juvenile hormone-like substances, melanotic tumors, Drosophila: 1194
- metals, human, review: 996
- nitroso compounds, transplacental, rodent, review: 1005
- review: 1019,1021
- steroid hormones, endocrine tumors, review: 999

CARCINOGENS, CHEMICAL

- antagonists and inhibitors, mechanism of action, review: 1008
- chromosomal abnormalities, classification, review: 1002
- DNA alkylation, mechanism, review: 1011
- dietary, g.i. and liver tumors, review: 1014
- mouse strain for testing very weak carcinogens: 1190
- screening
 - cell cultures, review: 1007
 - review (book): 1022,1023
- thymic lymphoma, possible leukemia virus, mouse: 1203

CELL GROWTH KINETICS

- asbestos-induced mesothelioma, mathematical model, rat: 1340
- effect of ethylsulfonylnaphthalene-1-sulfonamide, bladder, mouse: 1167
- human cancer, method of studying DNA synthesis: 1420
- methylcholanthrene-induced skin tumors, mouse: 1057
- normal and transformed cells, review: 1006
- relationship to catalase activity, rat hepatoma: 1341
- skin tumors or premalignant lesions, human: 1339

CELL GROWTH KINETICS, (Contd.)

- tobacco smoke-exposed mouse lung or kidney cells: 1211

CERVIX UTERI

- contraceptive hormone effects on nucleic acid and protein synthesis, human: 1425

CERVIX UTERI NEOPLASMS

- chromosomes: 1396
- epidemiology
 - India (southern): 1363
 - microinvasive carcinoma, Ohio (Cleveland): 1361
 - New York City, hormonal or mechanical contraceptives: 1387
 - Utah: 1352

induction

- dimethylbenzanthracene alone or + contraceptives, mouse: 1128
- possible, estrogen-progestagen contraceptive, human: 1127
- radiation and/or benzpyrene, mouse: 1036
- pre malignant dysplasia or carcinoma in situ, contraceptive hormone effects on DNA, RNA and protein: 1425

CHEEK POUCH NEOPLASMS

- induction, dimethylbenzanthracene, hamster: 1075,1076
- lymphoma-like, induction, vitamin A palmitate, hamster: 1164
- SV40-induced, pathology, hamster: 1281,1282

CHOLESTEROL

- effect on
 - methylcholanthrene tumors, mouse: 1064
 - protein synthesis, human WBC: 1192

CHROMOSOMES

- abnormalities
 - cervix cancer: 1396
 - human cancer, review: 1003,1010
 - Klinefelter's syndrome, breast cancer: 1400
 - leukemia superimposed on radiation-treated Hodgkin's disease: 1405
 - mongolism, lymphocyte transformation rate: 1402
 - with leukemia, possible leukemia virus, review: 1026
 - child: 1406
 - tobacco smoke-exposed mouse lung or kidney cells: 1211
- benzene-induced acute leukemia, human: 1120
- breakage, induction, radiation or radiomimetic compounds, plant: 1399
- carcinogen binding, rat liver: 1066
- effect of
 - carcinogens or viruses, mechanism, review: 1002
 - luteoskyrin, tumor cells: 1172
- griseofulvin-induced leukemia, human: 1201
- group 17/18, RES tumors, review: 1015
- methylcholanthrene-induced tumors
 - rat: 1053
 - skin, mouse: 1054
- Ph¹, Xg genotype, chronic myeloid leukemia: 1394,1398
- ploidy
 - endometrial carcinoma: 1395
 - melanoma: 1393

CHROMOSOMES, (Contd.)

- methyl dimethylaminoazobenzene rat hepatoma nuclei: 1141
- WBC, occupational radiation exposure: 1030
- radiation-induced leukemia
 - human: 1031
 - mouse: 1033
- spontaneous or benzo(a)pyrene-induced tumors, rat: 1053

CHRYSENE

- metabolism, effect of methylcholanthrene, rat liver microsomes: 1049

CINNAMALDEHYDE, 3,5-DIMETHOXY-4-HYDROXY-

- nasopharynx cancer, review: 1004

COCARCINOGEN A-1

- epidermal hyperplasia, mouse skin: 1188

COCARCINOGENESIS (See also Carcinogenesis)

- mechanism, review: 1020

COCARCINOGENS, CHEMICAL

- effect on threshold response to skin carcinogens, mouse: 1087

COLON

- familial polyposis (Peutz-Jeghers syndrome), sex cord tumor of ovary: 1403

COLON NEOPLASMS

- familial multiple polyposis: 1332

CONNECTIVE TISSUE NEOPLASMS

- epidemiology

Kaposi's sarcoma, Nigeria: 1371

rhabdomyosarcoma, children, Mexico City: 1362

familial cancer syndrome, children, U.S.: 1334

induction, methyl nitrosourea, dog: 1153

nickel sulfide-induced rhabdomyosarcoma, rat: 1177, 1178

radiation-induced, rabbit: 1028

spindle cell sarcoma, runtting syndrome, mouse: 1200

CONTRACEPTIVES, HORMONAL

cervix cancer, New York City: 1387

effect on nucleic acid and protein synthesis, human cervix: 1425

estrogen-progestagen type

benign fibrocystic disease of breast, human: 1126

breast cancer, human: 1125

cervix cancer, human: 1127

progestational agents, effect on dimethylbenzanthracene induction of cervix cancer, mouse: 1128

CONTRACEPTIVES, MECHANICAL

cervix cancer, New York City: 1387

COPPER

basic cupric acetate, effect on dimethylaminoazobenzene liver tumors, rat: 1137

CORPUS UTERI NEOPLASMS

choriocarcinoma and related diseases

epidemiology, Australia (Sydney): 1367

Iraq: 1366

endometrial cancer

chromosomes: 1395

high-risk groups, metabolic status: 1136, 1357, 1431

possibly radiation-induced, human: 1037

CORTICOSTERONE

effect on aflatoxin metabolism, rat liver microsomes: 1115

CORTISONE

effect on urethan lung tumors, mouse: 1081

CROTON OIL

epidermal hyperplasia, mouse skin: 1188

CYCASIN

carcinogenic and toxic effects, animal or human, review: 1017

toxicity, conventional or germ-free rat, review: 995

CYCASIN AGLYCONES

toxic and carcinogenic effects, animal or human, review: 1017

DIABETES MELLITUS

endometrial cancer: 1357, 1431

oropharynx cancer, U.S.: 1384

DIETARY FACTORS (See also Foods)

esophagus cancer, South Africa (Transkei), ethnic groups: 1121, 1122

excretion of tryptophan metabolites, Africa (Uganda): 1368

protein intake, stomach or intestinal cancer, international: 1432

DIETHYLSTILBESTROL

effect on aflatoxin liver carcinogenesis, rat: 1110

leiomyosarcoma of ductus deferens, hormone-independent variants, hamster: 1130

DIMETHYL SULFOXIDE

effect on dimethylbenzanthracene skin tumors, resistant mouse strain: 1079

DIOXANE

nasal cavity and liver tumors, rat: 1160

DISTRIBUTION

aflatoxin

monkey or human: 1113

rat: 1108, 1113

dibenzopyrene, mouse: 1170

dimethylbenzanthracene, mammary gland, effect of oophorectomy or hypophysectomy, rat: 1212

Moloney sarcoma virus, newborn mouse: 1304

nucleic acids and nucleases, Friend leukemia virus-infected mouse spleen: 1306

DODECYL METHYL ETHER

juvenile hormone activity and tumor induction, *Drosophila*: 1194

DUCTUS DEFERENS NEOPLASMS

androgen- or estrogen-induced, hormone-independent variants, hamster: 1130

DUST

carbon black or rubber, effect on tumor cells or tobacco callus *in vitro*: 1124

coal, occupational exposure, chronic bronchitis, smoking, Germany: 1117

EB VIRUS (See under Virus, herpes-type)

ENDOCRINE ABLATION

oophorectomy or hypophysectomy, effect on dimethylbenzanthracene uptake, rat mammary gland: 1212

ENDOCRINE ABLATION, (Contd.)

- orchiectomy
 - effect on
 - benzpyrene-induced brain tumors, rat: 1094
 - dimethylbenzanthracene tumors, hamster cheek pouch: 1076

ENDOTOXINS, BACTERIAL

- runting syndrome, tumor induction, mouse: 1200

ENVIRONMENTAL FACTORS

- asbestos exposure, review: 1018
- cancer epidemiology, migrant populations, international: 1338
- geographical variations in temperature, cancer mortality, U.S.: 1342
- isolation or crowding, effect on dimethylbenzanthracene mammary tumors, rat: 1070
- oropharynx cancer, U.S.: 1384
- seasonal solar activity, leukemia, Poland (Cracow): 1392
- stomach cancer (intestinal metaplasia type), Colombia (Cali), migrants: 1390

ENZYMES

- alkaline phosphatase or nonspecific esterase, methylcholanthrene-induced brain sarcoma, mouse: 1051
- aminoacyl-tRNA synthetase, effect of benzanthrene and phenanthrene compounds, cell-free system: 1184
- arginase, nickel sulfide-induced rhabdomyosarcoma, rat: 1177
- benzpyrene hydroxylase, effect of aflatoxin or benzpyrene, rat liver microsomes: 1116
- catalase, relation to growth rate, rat hepatoma: 1341
- DOPA oxidase, melanocytes of methylcholanthrene- or dimethylbenzanthracene-induced skin tumors, mouse: 1067
- fructose phosphate aldolase, diethylnitrosamine-induced liver damage, rat: 1148
- RNA polymerase, RNA-dependent, virus-induced avian myeloblastosis: 1230
- thymidine triphosphate pathway, methyl-dimethylaminoazobenzene liver tumors, rat: 1142
- transfer RNA methylase, GA (Marek's disease-associated) virus-induced liver tumor, chick: 1319
- trypsin esterase, binding, radiation-leukemia protection factor, sheep spleen or serum extracts: 1035

EPIDEMIOLOGY

- all tumors
 - aged, Germany (Magdeburg): 1372
 - children, Bulgaria: 1378
 - Czechoslovakia (České Budějovice district): 1376
 - environmental temperature, geographical variations, U.S.: 1342
 - Finland: 1380
 - Hong Kong (Chinese): 1382
 - infants and children, Hungary: 1348
 - migrant populations, international: 1338
 - sex ratio, England/Wales and western Europe: 1389

EPIDEMIOLOGY, (Contd.)

- asbestos bodies in lungs, Michigan (Detroit and Lower Peninsula): 1102
- asbestos exposure, environmental review: 1018
- biliary tract cancer, Germany (Göttingen-Weende): 1360
- bladder cancer
 - exposure to aromatic amines, rubber industry, Britain: 1119
 - smoking, U.S.: 1337
- bone tumors, radiation exposure, Hiroshima/Nagasaki: 1027
- brain tumors, review: 992
- breast cancer
 - age factors, international: 1388
 - cancer, environmental temperature, geographical variations, U.S.: 1343
 - infants and children, Canada (Ontario): 1346
 - lactation and reproductive histories, Massachusetts (Boston): 1356
 - male, Finland: 1379
 - Klinefelter's syndrome: 1400
 - Minnesota (Minneapolis): 1344
 - Oklahoma, ethnic groups: 1353
 - reproductive history, Wales (southern): 1385
- bronchitis, smoking, coal miners, Germany: 1117
- cervix cancer
 - hormonal or mechanical contraceptives, New York City: 1387
 - India (southern): 1363
 - microinvasive, Ohio (Cleveland): 1361
 - Utah: 1352
- choriocarcinoma and related diseases
 - Australia (Sydney): 1367
 - Iraq: 1366
- chronic toxic symptoms, occupational arsenic exposure, Poland (Zloty Stok): 1118
- endometrial cancer
 - hormonal status: 1357, 1431
 - identification of high-risk groups, estrogen metabolism: 1136
- esophagus cancer
 - central Africa (Zambia and Malawi), alcoholic beverages: 1122
 - Kenya (western): 1369
 - South Africa (Transkei), ethnic groups, dietary factors: 1121
 - sex difference: 1386
- Fallopian tube cancer, New York (Long Island): 1358
- female genital cancer, Oklahoma, ethnic groups: 1353
- gallbladder cancer
 - Germany (Göttingen-Weende): 1360
 - Poland (Warsaw), cholecystitis: 1350
- g.i. cancer, environmental temperature, geographical variations, U.S.: 1343
- intestinal cancer
 - dietary protein, international: 1432
 - risk of multiple primary cancer: 1359
- Kaposi's sarcoma, Nigeria: 1371
- kidney cancer
 - phenacetin abuse, Sweden: 1123

EPIDEMIOLOGY, (Contd.)

- smoking, U.S.: 1337
- leukemia
 - children
 - California (Los Angeles): 1345
 - Canada (Saskatchewan): 1377
 - familial, Nebraska: 1333
 - mongolism, Massachusetts: 1335
 - Poland, dermatoglyphic patterns: 1391
 - Gc blood groups: 1397
 - seasonal solar activity, Cracow: 1392
 - review: 1016
- liver tumors
 - dietary carcinogens, review: 1014
 - Uganda: 1374
- lung cancer
 - Italy (Genoa): 994
 - methods, review: 994
 - smoking, ^{210}Po content of tobacco, review: 1024
 - U.S.: 1337
 - Utah: 1351
- lymphoma
 - Epstein-Barr virus-positive: 1255
 - familial, Nebraska: 1333
 - lymphoma, review: 1016
- melanoma, Australia (Queensland), geographical variation, sun exposure: 1381
- mouth cancer
 - environmental factors and ethnic groups, U.S.: 1384
 - methods, review: 990
 - smoking, U.S.: 1337
- multiple primary tumors
 - risk, stomach or intestinal cancer: 1359
 - West Virginia: 1354
- myeloma, Minnesota (Olmsted County): 1349
- nasopharynx cancer, sinapylaldehyde exposure, international, review: 1004
- pharynx cancer, U.S., environmental factors and ethnic groups: 1384
- pleural mesothelioma, asbestos exposure, West Germany (Hamburg): 1370
- prostate cancer, Oklahoma, ethnic groups: 1353
- respiratory cancer
 - environmental temperature, geographical variations, U.S.: 1343
 - smoking, U.S.: 1337
- rhabdomyosarcoma, children, familial cancer syndrome, U.S.: 1334
- serum Epstein-Barr virus antibodies, young adults, U.S.: 1256
- skin cancer
 - Germany (Giessen), age factors: 1365
 - India (Saurashtra): 1364
 - Minnesota: 1355
- soft tissue sarcomas, children, Mexico City: 1362
- solid tumors, children, Japan (Nagoya): 1347
- stomach cancer
 - dietary carcinogens, review: 1014
 - protein, international: 1432
 - intestinal metaplasia type, Colombia (Cali), ethnic groups: 1390
 - Poland (urban and nationwide): 1373, 1375

EPIDEMIOLOGY, (Contd.)

- risk of multiple primary cancer: 1359
- urinary tryptophan metabolites, dietary factors, Africa (Uganda): 1368
- EPIDEMIOLOGY, VETERINARY
 - latent SV40 or foamy virus infection, primate colony: 1276
 - parainfluenza-like virus infection, squirrels (Britain), hamster tumor induction: 1299
 - thyroid cancer and parathyroid hyperplasia, strain differences, rat: 1433
- EPOXIDES
 - mechanism of action, animal, review: 1001
- ESOPHAGUS NEOPLASMS
 - epidemiology
 - alcoholic beverages, central Africa (Zambia and Malawi): 1122
 - Kenya (western): 1369
 - South Africa (Transkei), ethnic groups, dietary factors: 1121
 - sex difference: 1386
 - following gastrectomy or gastroenterostomy: 1045
- ESTRADIOL
 - leiomyosarcoma of ductus deferens, hormone-independent variants, hamster: 1130
 - metabolism, high-endometrial cancer-risk women: 1136
- ESTRADIOL VALERATE
 - pituitary tumors, mouse: 1129
- ESTRADIOL, ETHYNYL-
 - effect on dimethylbenzanthracene induction of cervix cancer, mouse: 1128
- ETHERS, HALOGENATED
 - mechanism of action, animal, review: 1001
- ETHNIC GROUPS
 - breast, prostate or female genital cancer, Oklahoma: 1353
 - cancer incidence, migrant populations, international: 1338
 - esophagus cancer, South Africa (Transkei): 1121, 1386
 - oropharynx cancer, U.S.: 1384
 - stomach cancer (intestinal metaplasia type), migrants, Colombia (Cali): 1390
- ETHIONINE
 - liver tumors
 - methylation of transfer or ribosomal RNA, rat: 1144
 - specific biochemical abnormalities, rat: 1173
- FARNESYL METHYL ETHER
 - juvenile hormone activity and tumor induction, *Drosophila*: 1194
- FLUORENE, N-HYDROXY-2-AMINO-
 - mutagenesis (bacteria) and skin tumor-initiating effect (mouse): 1183
- N-2-FLUORENYLACETAMIDE
 - bladder tumors, effect of bladder parasite, rat: 1171
 - effect on WBC phagocytic activity, rat: 1180
 - s.c. and kidney sarcomas and liver tumors, synergism with polyoma virus, rat: 1202

- N-2-FLUORENYLACETAMIDE, N-ACETOXY-
mutagenesis (bacteria) and skin tumor-initiating
effect (mouse): 1183
- N-2-FLUORENYLACETAMIDE, N-HYDROXY-
mutagenesis (bacteria) and skin tumor-initiating
effect (mouse): 1183
- FOODS (See also under Dietary factors)
carcinogens, g.i. or liver tumors, animal or
human, review: 1014
meats, aflatoxin content: 1104,1105
- GA VIRUS (See under Virus, herpes-type)
- GALLBLADDER NEOPLASMS
epidemiology
Germany (Göttingen-Weende): 1360
Poland (Warsaw), cholecystitis: 1350
- GASTROINTESTINAL CARCINOGENESIS
benzpyrene, effect of vitamin A, hamster:
1089
dietary carcinogens, animal, review: 1014
diethylnitrosamine, mouse: 1147
methylnitrosourea, intestine, hamster: 1154
- GASTROINTESTINAL NEOPLASMS
DNase and RNase activity, susceptible sites,
human: 1424
epidemiology
environmental temperature, geographical
variations, U.S.: 1343
sex ratio, England/Wales and western Europe:
1389
- GENETICS, ANIMAL
Friend leukemia virus susceptibility, site of
susceptibility locus, mouse bone marrow
cells: 1217
guinea pig strain susceptible to L2C/NB
leukemia, herpes-type virus isolation:
1328
mammary tumor virus-positive mouse strain,
low spontaneous mammary tumor incidence:
1253
mouse strain highly susceptible to very weak
carcinogens: 1190
skin tumor susceptibility or resistance,
epidermal cell endoplasmic reticulum,
mouse: 1422
strain differences
dimethylbenzanthracene salivary gland
tumors, rat: 1073
leukemia virus infection, mouse: 1305
thyroid cancer or parathyroid hyperplasia
incidence, rat: 1433
- GENETICS, HUMAN
Chediak-Higashi syndrome, abnormal peripheral
WBC cultures: 1407
chromosome abnormalities and cancer risk,
review: 1010
familial
cancer: 1331
syndrome associated with childhood
rhabdomyosarcoma: 1334
Christchurch chromosome (Gp⁻), mongolism
and leukemia: 1336
freckling patterns and neurofibromatosis:
1413
leukemia and lymphoma, Nebraska: 1333
- GENETICS, HUMAN, (Contd.)
SV40-transformation susceptibility of
skin fibroblasts: 1225
polyposis of colon, intestinal cancer:
1332
sex cord tumor of ovary: 1403
Gc group distribution, leukemia, Poland: 1397
kidney tumors, siblings: 1409
melanoma, identical twins: 1330
mongolism
acute leukemia, possible leukemia virus,
review: 1026
leukemia and other malformations,
Massachusetts: 1335
pheochromocytoma, identical twin: 1408
Xg genotype, Ph⁺-positive or -negative chronic
myeloid leukemia: 1394,1398
- GENETICS, MICROBIAL
SV40 genome, monkey-mouse hybrid cell lines:
1278
- GENITAL NEOPLASMS, FEMALE
epidemiology, ethnic groups, Oklahoma: 1353
Fallopian tube tumors, epidemiology, New York
(Long Island): 1358
- GERM-FREE STATUS
effect on
autoimmunity and lymphoma, NZB mice: 1430
cycasin toxicity, rat, review: 995
leukemoid reaction with Rous viral sarcoma,
rat: 1301
mineral oil induction of plasma cell tumors,
mouse: 1175
spontaneous transformation, rat embryo cells:
1296
- GLUCOSAMINES
membrane
normal mouse cells: 1287
virus-transformed mouse or hamster cells:
1287,1324
- GRISEOFULVIN
leukemia, human: 1201
- GUANINE 3-N-OXIDE
s.c. tumors, rat: 1189
- HEART.NEOPLASMS
pericardial mesothelioma, asbestos induction,
rat: 1101
- HISTAMINE
antagonists and inhibitors, effect on protein
synthesis, rat tumors: 1243
- HORMONES
effect on methylcholanthrene-induced prostate
tumors, rat: 1052
growth hormone, effect on methylcholanthrene
skin tumors, mouse: 1055
hydrocortisone and androgen metabolites,
breast cancer: 1412
insect, juvenile hormone-like substances,
melanotic tumor induction, Drosophila:
1194
metabolic status, cancer of endometrium:
1136,1357,1431
- HORMONES, CONTRACEPTIVE
cervix cancer, New York City: 1387
effect on nucleic acids and protein, human
cervix: 1425

HORMONES, CONTRACEPTIVE, (Contd.)

- estrogen-progestagen
 - benign fibrocystic breast disease, human: 1126
 - breast cancer, human: 1125
 - cervix cancer, human: 1127
- progestational, effect on cervix cancer
 - induction, mouse: 1128

HORMONES, STEROID

- effect on protein synthesis, human WBC: 1192
- endocrine and other tumors, animal, review: 999

HYDRAZINE, 1,1-DIMETHYL-

- alkylating action, rat tumor: 1146

HYDROCARBONS, POLYCYCLIC AROMATIC

- mechanism of action, theoretical model: 1084

HYDROXYLAMINE

- effect on DNA, bacteriophage: 1168

IMMUNE SERUM

- antithymocyte serum, stimulation of plasma cell
 - tumors, mouse: 1197

IMMUNITY

cellular

- bovine papilloma virus-transformed rodent
 - embryo cells: 1270
- Rous sarcoma virus-induced rat tumors: 1244
- structure and antigenic activity of plasma
 - membrane lipids, tumor cells: 1429
- surface antigens
 - herpesvirus-infected cells: 1325
 - polyoma virus-infected hamster cells: 1273
 - transformed cells: 1324,1325
 - SV40-transformed or tumor cells: 1322,1323,1324
- SV40 coat protein antigen, nonpermissive
 - nuclei, heterokaryocyte cultures: 1277
- T antigen distribution, adenovirus 12-
 - induced hamster tumors: 1266
- transplantation antigens and viral carcinogenesis, animal and human, review: 1009
- tumor mitochondria-specific antigen(s),
 - rat hepatoma and tumor-bearing rat
 - liver cell mitochondria: 1435
- virus-specific antigens
 - carcinogen- or radiation-induced thymic
 - lymphoma, mouse: 1203
 - Rous sarcoma virus-transformed hamster
 - cells: 1313

host

- effect of thymectomy, thymoma-bearing mouse: 1198
- immunogenicity, spontaneous or induced
 - tumors, mouse: 1248
- loss of serum opsonin activity, human
 - cancer: 1416
- methylcholanthrene-induced tumors, animal: 1063,1209
- Rous sarcoma virus-induced rat tumors: 1244
- serum immunoglobulins, chicken with Marek's
 - disease: 1258
- skin isograft, effect of leukemia virus,
 - mouse: 1227

IMMUNITY, (Contd.)

- thymus and leukemogenesis, review: 991

IMMUNITY DISORDERS

autoimmunity

- malignant transformation, germ-free NZB
 - mice: 1430
- virus infection, cancer pathogenesis,
 - review: 1025

- chimerism, induction, methylcholanthrene +
 - irradiation, rat: 1046

- graft-versus-host reaction, lymphoma incidence,
 - mouse: 1199

- runting syndrome, tumor induction, mouse: 1200

IMMUNOSUPPRESSION

- Friend-associated virus (Rowson-Parr virus),
 - mouse: 1216

- Rauscher leukemia virus, mouse: 1219,1318

INJURIES (See also Scar tissue and Stress)

- bone, sarcoma, Paget's disease: 1404

INSECTS

- Drosophila, melanotic tumor strain, tumor
 - induction by juvenile hormone-like substances: 1194

INTERFERON

- effect on leukemia incidence and radiation-
 - induced kidney disease, RF/Un mice: 1040

INTERFERON INDUCTION (See also Statolon)

effect on

- Friend leukemia virus infection, mouse: 1321

- Moloney sarcoma or Friend leukemia virus
 - in vitro: 1235

INTESTINE, LARGE, NEOPLASMS

- epidemiology, dietary protein, international: 1432

- risk of multiple primary tumors: 1359

INTESTINE, SMALL, NEOPLASMS

- malignant transformation of regional enteritis: 1410

ISONICOTINIC ACID HYDRAZIDE

- absence of carcinogenic effect, animal or
 - human: 1159

ISOTHIOCYANATE, ALLYL-

- epidermal hyperplasia, mouse skin: 1188

ISOTHIOCYANATE, α -NAPHTHYL-

- liver tumors, specific biochemical abnormalities, rat: 1173

KIDNEY

- radiation-induced glomerulosclerosis,
 - relationship to leukemia, RF/Un mouse
 - strain: 1040

KIDNEY CARCINOGENESIS

- dimethylnitrosamine, rat: 1145
- polyoma virus + fluorenylacetamide, synergism,
 - rat: 1202

KIDNEY NEOPLASMS

epidemiology

- phenacetin abuse, Sweden: 1123
- smoking, U.S.: 1337

- Wilms' tumor or metanephric hamartoma,
 - siblings: 1409

LACTATION

breast cancer epidemiology, Massachusetts (Boston): 1356

LACTONES

mechanism of action, animal, review: 1001

LEAD ACETATE

endocrine tumors, rat: 1131

LEUKEMIA, EXPERIMENTAL

cell-transmitted, properties, mouse: 1228

human-type acute lymphoblastic, Opler virus-induced, guinea pig: 1226

incidence, effect of radiation and interferon, RF/Un mouse strain: 1040

L2C/NB (guinea pig), herpes-type virus

isolation, susceptible guinea pig strain: 1328

Mycoplasma neurolyticum-infected mice: 1232

spontaneous, Fischer rat: 1229

LEUKEMIA, HUMAN

aging, review: 1013

chromosome abnormalities, review: 1010

chronic granulocytic, griseofulvin-induced, chromosomes: 1201

lymphocytic, lymphocyte transformation capacity: 1423

epidemiology

children

California (Los Angeles): 1345

Canada (Saskatchewan): 1377

Hungary: 1348

Poland, dermatoglyphic patterns: 1391

Gc blood group distribution: 1397

seasonal solar activity, Cracow: 1392

review: 1016

familial, Nebraska: 1333

SV40-transformation susceptibility of skin fibroblasts: 1225

mongolism

chromosome abnormalities, child: 1406

Christchurch (Gp⁻) chromosome, familial: 1336

frequency of associated malformations, children, Massachusetts: 1335

possible leukemia virus, review: 1026

mouse-transmitted, properties: 1228

pathogenesis, role of thymus, review: 991

Ph¹-positive or -negative chronic myeloid leukemia, Xg genotype: 1394, 1398

LEUKEMIA VIRUS (See Virus, leukemia/lymphoma)

LEUKEMOGENESIS, EXPERIMENTAL

methylcholanthrene, mouse: 1228

methylnitrosourea, lymphoma, mouse: 1185

mineral oil, germ-free or conventional mice: 1175

role of thymus, review: 991

saponin, rabbit: 1163

spleen cells inducing graft-host reaction, mouse: 1199

treatments causing runtting syndrome, mouse: 1200

urethan lymphoma

effect of thymectomy, mouse: 1083

tumor cell DNA, mouse: 1080

viral, leukemia virus cytotropism, review: 1012

LEUKEMOGENESIS, HUMAN

occupational benzene exposure, chromosomal abnormalities: 1120

griseofulvin: 1201

LEUKEMOID REACTION

Rous virus-induced sarcoma, germ-free rat: 1301

LIPIDS

composition, adenovirus 12-induced hamster tumors: 1264

plasma membrane, structure and antigenic activity, tumor cells: 1429

LIVER

aromatic hydrocarbon breakdown in vitro,

effect of methylcholanthrene, rat: 1049

chromatin or DNA, methylcholanthrene or

benzpyrene binding, rat: 1066

microsomes

effect of

aflatoxin, animal: 1114, 1115, 1116

benzpyrene, rat: 1090, 1116

methylcholanthrene, animal: 1060, 1061,

1062, 1091, 1205, 1206, 1207

zoxazolamine metabolism, effect of 6-

substituted benzpyrene derivatives, rat: 1092

mitochondria and microsomes, specific

metabolic abnormalities, α -naphthylisothiocyanate or ethionine hepatoma, rat:

1173

polyribosomal protein synthesis, effect of

tannic acid, rat: 1179

regeneration, effect of dimethylbenzanthracene,

mouse: 1204

RNA synthesis, effect of nickel carbonyl, rat:

1176

toxicity, diethylnitrosamine, fructose

phosphate aldolase, rat: 1148

LIVER CARCINOGENESIS

aflatoxin (rat)

effect of diethylstilbestrol: 1110

methylation of transfer or ribosomal RNA: 1144

tumor histology and enzyme histochemistry: 1111

o-aminoazotoluene, morphology of premalignant tumors, mouse: 1169

cycasin and its aglycone, mechanism, review: 1017

dietary carcinogens, animal, review: 1014

diethylnitrosamine

effect of partial hepatectomy, rat: 1149

mouse: 1147

dimethylaminoazobenzene (rat)

effect of

copper salt: 1137

riboflavin or antitumor antibiotic on

liver phospholipids: 1139

establishment of new ascites hepatomas: 1140

pentose phosphate metabolism: 1138

dimethylnitrosamine

mouse: 1185

rat: 1145

LIVER CARCINOGENESIS, (Contd.)

methylation of ribosomal or transfer

RNA: 1144

dioxane, rat: 1160

ethionine (rat)

methylation of transfer or ribosomal RNA:
1144

specific biochemical abnormalities: 1173

methyl dimethylaminoazobenzene (rat)

nuclear fractionation by ploidy: 1141

nucleolar 45S and 28S RNA composition:
1143

thymidine triphosphate metabolism: 1142

 α -naphthylisothiocyanate, specific biochemical
abnormalities, rat: 1173

nitroso compounds, mechanism, review: 998

polyoma virus + fluorenylacetamide, synergism,
rat: 1202

LIVER DISEASES

alcoholic cirrhosis, malignant transformation:
1415

cirrhosis, oropharynx cancer, U.S.: 1384

LIVER NEOPLASMS

aflatoxin metabolism, human: 1113

epidemiology

dietary carcinogens, review: 1014

Uganda: 1374

GA (Marek's disease-associated) virus-induced,
transfer RNA methylase, chick: 1319malignant transformation of alcoholic cirrhosis:
1415relationship of growth rate to catalase, rat
hepatoma: 1341

Taper hepatoma (mouse), RNA synthesis: 1427

transplanted rat hepatomas, tumor mitochondria-
specific mitochondrial antigen(s): 1435

JUNG

isoniazid toxicity, animal or human: 1159

tuberculosis, pneumothorax with fluoroscopy,
breast cancer incidence, human: 1042

JUNG CARCINOGENESIS

asbestos, rat: 1101

benzpyrene, effect of vitamin A, hamster:
1089

diethylnitrosamine, mouse: 1147

dimethylbenzanthracene + radiation, mouse:
1039

ethylnitrosourea, transplacental, mouse: 1152

methylnitrosamines and methylnitrosamides,
mouse: 1185

urethan (mouse)

effect of

butyl or isoamyl carbamate: 1082

cortisone: 1081

radiation: 1039, 1081

thymectomy: 1083

JUNG NEOPLASMS

bronchogenic carcinoma, nuclear DNA content:
1426

epidemiology

Italy (Genoa): 994

methods, review: 994

smoking, ^{210}Po content of tobacco, review:
1024

U.S.: 1337

Utah: 1351

LUNG NEOPLASMS, (Contd.)

isoniazid-treated TB, human: 1159

lung scar cancer, pathology, human: 1043, 1044

serum and tissue cadmium and zinc: 1135

LUTEOSKYRIN

effect on DNA and chromosomes, tumor cells:
1172

LYMPH NODE

non-lymphomatous hyperplasia, leukemia virus-

like particles, human: 1233

LYMPHOMA, MALIGNANT, EXPERIMENTAL

induction

spleen cells inducing graft-host reaction,
mouse: 1199treatments causing runtting syndrome, mouse:
1200*Mycoplasma neurolyticum*-infected mice: 1232

NZB mice, effect of germ-free status: 1430

radiation- or carcinogen-induced, possible
leukemia virus, mouse: 1203

LYMPHOMA, MALIGNANT, HUMAN

Burkitt type

cell lines (EB virus-positive or -negative),

DNA synthesis, temperature effects: 1257

cell-transmitted mouse leukemia, properties:
1228

epidemiology, review: 1016

Epstein-Barr virus, isolation, properties and
geographical distribution: 1255

familial, Nebraska: 1333

Hodgkin's disease

DNA induction of virus formation, HeLa
cells: 1294possible radiation-induced myeloid
leukemia, chromosome abnormalities:
1405

MALIGNANT TRANSFORMATION

alcoholic cirrhosis to carcinoma of liver:
1415

benign syphilis to cancer of penis: 1401

cell cultures, relationship to tumor develop-
ment, review: 1006hidradenitis suppurativum to carcinoma of
skin: 1417

lymphocyte cultures

chronic lymphocytic leukemia: 1423

mongolism: 1402

normal persons: 1414

methylcholanthrene-exposed mouse prostate
culture: 1065Paget's disease of bone, sarcoma at site of
injury: 1404polyposis to cancer of colon and rectum,
familial: 1332rat embryo cell cultures, nitroquinoline oxide:
1166regional enteritis to cancer of small
intestine: 1410scar tissue to cancer of lung, pathology,
human: 1043, 1044

spontaneous, germ-free rat embryo cells: 1296

MAMMARY CARCINOGENESIS, EXPERIMENTAL

dimethylbenzanthracene

effect of

isolation or crowding, rat: 1070

- MAMMARY CARCINOGENESIS, EXPERIMENTAL, (Contd.)
 melatonin or environmental light, rat: 1041
 surgical trauma (mastectomy), rat: 1071
 mammary tumor virus-positive, low spontaneous-mammary tumor mouse strain: 1253
- MAMMARY CARCINOGENESIS, HUMAN
 estrogen-progestagen contraceptives: 1125
 benign fibrocystic disease: 1126
 radiation (pulmonary fluoroscopy for TB): 1042
- MAMMARY GLAND
 dimethylbenzanthracene uptake, effect of oophorectomy or hypophysectomy, rat: 1212
 DNA, effect of dimethylbenzanthracene, sex difference, rat: 1069
- MAMMARY NEOPLASMS, EXPERIMENTAL
 low-tumor incidence, high-MTV mouse strain: 1253
 S3C carcinoma (mouse), spontaneous, immunogenicity, mouse: 1248
- MAMMARY NEOPLASMS, HUMAN
 epidemiology
 age factors, international: 1388
 environmental temperature, geographical variations, U.S.: 1343
 ethnic groups, Oklahoma: 1353
 infants and children, Canada (Ontario): 1346
 Minnesota (Minneapolis): 1344
 pulmonary fluoroscopy for TB: 1042
 reproductive histories, Massachusetts (Boston): 1356
 Wales (scutern): 1385
 hormone excretion and psychological factors: 1412
 male, epidemiology, Finland: 1379
 Klinefelter's syndrome: 1400
- MAREK'S DISEASE (See also under Virus, herpes-type)
 serum immunoglobulins, chicken: 1258
- MAREK'S DISEASE VIRUS (See under Virus, herpes-type)
- MELANOMA, MALIGNANT
 chromosome abnormalities: 1393
 epidemiology, geographical variations, Australia (Queensland), sun exposure: 1381
 identical twins: 1330
 intranuclear virus-like inclusion bodies, human: 1292
- MELATONIN
 effect on dimethylbenzanthracene mammary tumors, rat: 1041
- METABOLISM (glycolysis and respiration)
 pentose phosphate pathway, dimethylamino-azobenzene liver tumors, rat: 1138
- METALS, HEAVY
 carcinogenesis, human, review: 996
- METHANESULFONATE, METHYL-
 effect on RNA, rat liver: 1157
 mutagenesis, *Neurospora*: 1158
- METHYLAZOXYMETHANOL (See Cycasin aglycone)
- 3-METHYLCHOLANTHRENE
 binding to chromatin or DNA, rat liver: 1066
 brain tumors (mouse): 1048, 1051
 virus-like particles: 1297
 chimera induction, irradiated rat: 1046
 + croton oil, skin tumors, DNA content and chromosomes, mouse: 1054
- 3-METHYLCHOLANTHRENE, (Contd.)
 effect on
 aromatic hydrocarbon breakdown, rat liver: 1049
 liver microsomes, animal: 1060, 1061, 1062, 1091
 protein synthesis, human WBC: 1192
 RNA transcription, rat liver: 1208
 epidermal tumors, amphibia (*Bufo arenarum*): 1056
 intestinal absorption, mechanism, animal: 1213
 leukemia, mouse: 1228
 metabolism, rat liver: 1205, 1206, 1207
 ovarian tumors, rabbit: 1047
 premalignant epidermal hyperplasia, mouse skin: 1188
 prostate tumors, hormone effects, rat: 1052
 sarcoma, immunogenicity, mouse: 1248
 s.c. tumors
 attempted induction, cattle: 1068
 effect of phospholipids or cholesterol, mouse: 1064
 host immunity, mouse: 1063
 skin tumors (mouse): 1078
 cell growth kinetics: 1057
 DOPA oxidase-positive melanocytes: 1067
 effect of growth hormone: 1055
 thalidomide; mouse: 1058
 solid or ascites tumors, chromosomes, rat: 1053
 thyroiditis, rat: 1050
 transformation, mouse prostate cultures: 1065
 transplantable mouse sarcoma, effect of guinea pig RNA: 1059
 tumor-specific transplantation antigens, mouse: 1209
- MITOMYCIN C (See under Antitumor agents)
- MOUTH NEOPLASMS
 epidemiology, screening methods, review: 990
 pigmented epithelial tumor of maxilla, infant, ultrastructure: 1419
- MUTAGENESIS
 alkylating carcinogens, *Neurospora*: 1158
 aminofluorene and naphthalene compounds, bacteria: 1183
 azobenzene or benzanthracene carcinogens, *Drosophila*: 1182
Mycoplasma neurolyticum
 infection, leukemia frequency, mouse: 1232
- MYELOMA AND RELATED DISEASES
 epidemiology, Minnesota (Olmsted County): 1349
 MOPC-31B mouse myeloma, myeloma protein synthesis in vitro: 1428
 MPC-37 or MOPC-104E plasmacytoma (mouse), stimulation, antithymocyte serum: 1197
 mouse plasmacytoma
 adjuvant-induced, leukemia virus-like particles: 1298
 mineral oil-induced, germ-free mice: 1175
 leukemia virus-like particles: 1250, 1251
- NAPHTHALENE, N-ACETOXY-1-ACETYLAMINO-
 mutagenesis (bacteria) and skin tumor-initiating effect (mouse): 1183

- APHTHALENE, N-ACETOXY-2-ACETYLAMINO-
mutagenesis (bacteria) and skin tumor-initiating
effect (mouse): 1183
- APHTHALENE, 1-HYDROXY-2-AMINO-
mutagenesis (bacteria) and skin tumor-initiating
effect (mouse): 1183
- APHTHALENE, N-HYDROXY-1-AMINO-
mutagenesis (bacteria) and skin tumor-initiating
effect (mouse): 1183
- APHTHALENE, N-HYDROXY-2-AMINO-
mutagenesis (bacteria) and skin tumor-initiating
effect (mouse): 1183
- APHTHALENE-1-SULFONAMIDE- 4-ETHYLSULFONYL-
bladder tumors, mouse: 993
effect on bladder cell growth rate, mouse:
1167
- ASAL CAVITY NEOPLASMS
dioxane induction, rat: 1160
- ASOPHARYNX NEOPLASMS
epidemiology
occupational, review: 1004
sinapylaldehyde exposure, international,
review: 1004
- EOPLASMS, EXPERIMENTAL
adenovirus 12-induced (hamster), DNA or lipid
composition: 1263, 1264
AH-7974 hepatoma (rat), DNA and RNA, effect of
nitrosoguanidine derivative: 1151
benzpyrene- or methylcholanthrene-induced
mouse sarcomas, effect of guinea pig tissue
RNA: 1059
bovine papilloma virus-induced, pathology,
cattle, horses and rodents: 1269
Ehrlich carcinoma (mouse), cells, effect of
luteoskyrin on DNA and chromosomes: 1172
hepatoma, tumor mitochondria-specific
mitochondrial antigen(s), rat: 1435
pathogenesis, cell transformation, review:
1006
rat tumors, effect of histidine decarboxylase
inhibitors on protein synthesis: 1243
Rauscher leukemia virus-induced hamster tumor,
properties of virus: 1220
Sarcoma 37 or 180 (mouse), malignancy-
associated changes in peripheral WBC: 1434
spontaneous or induced (methylcholanthrene or
benzpyrene), ascites or solid, chromosomes,
rat: 1053
Yoshida sarcoma (rat), effect of possible
dimethylnitrosamine metabolite: 1146
- EOPLASMS, HUMAN
autoimmunity and virus diseases, review: 1025
chromosome abnormalities, review: 1003, 1010
epidemiology
aged, Germany (Magdeburg): 1372
children, Bulgaria: 1378
Czechoslovakia (České Budějovice district):
1376
environmental temperature, geographical
variations, U.S.: 1342
Finland: 1380
Hong Kong (Chinese): 1382
migrant populations, international: 1338
familial: 1331
multiple primary, epidemiology, West Virginia:
1354
- NEOPLASMS, HUMAN, (Contd.)
psychosomatic aspects: 1411
RNA virus-like particles: 1293
serum adenovirus-18 antibodies: 1261
loss of opsonin activity: 1416
and tissue cadmium and zinc: 1135
solid tumors (neural, angiomatous, teratomatous
or embryonal), children, Japan (Nagoya):
1347
- NICKEL CARBONYL
effect on RNA, rat liver: 1176
- NICKEL SULFIDE
rhabdomyosarcoma, ultrastructure and enzymes,
rat: 1177, 1178
- NITROSAMINE, DIETHYL-
liver tumors
effect of partial hepatectomy, rat: 1149
mouse: 1147
lung and stomach tumors, mouse: 1147
toxicity, liver, fructose phosphate aldolase,
rat: 1148
- NITROSAMINE, DIMETHYL-
alkylating action of possible metabolite
(1,1-dimethylhydrazine), rat tumor: 1146
kidney and liver tumors, rat: 1145
liver tumors, methylation of transfer or
ribosomal RNA, rat: 1144
lung and liver tumors, mouse: 1185
- 4-NITROQUINOLINE-1-OXIDE
reaction with nicotinamide, mechanism: 1181
transformed rat embryo cells, s.c. sarcoma,
rat: 1166
- N-NITROSOGUANIDINE, N-NITRO-
chromosome breakage, plant: 1399
- N-NITROSOGUANIDINE, N-METHYL-N'-NITRO-
effect on DNA and RNA, rat hepatoma: 1151
mutagenesis, *Neurospora*: 1158
- NITROSO-p-TOLYLSULFONAMIDE, METHYL-
lung tumors, mouse: 1185
- N-NITROSOUREA, N-ETHYL-
lung tumors, fetal mouse: 1152
- N-NITROSOUREA, N-METHYL-
brain and soft tissue tumors, dog: 1153
effect on DNA, cell-free system: 1150
intestinal adenocarcinoma, hamster: 1154
lung tumors and lymphoma, mouse: 1185
mechanism of action, bacteria and tumor cells:
1155
- N-NITROSOUREA, N-METHYL-, 2-DEOXY-D-GLUCOSE
DERIVATIVE (streptozotocin)
mechanism of action, bacteria and tumor cells:
1155
- N-NITROSOURETHAN, N-METHYL-
effect on DNA, cell-free system: 1150
lung tumors, mouse: 1185
mechanism of action, bacteria and tumor cells:
1155
- NITROSO COMPOUNDS
liver tumors, mechanism, review: 998
transplacental tumor induction
brain, rat: 1191
rodent, review: 1005
- NUCLEASES
distribution, Friend leukemia virus-infected
mouse spleen: 1306
acid and alkaline DNase and RNase, cancer-
susceptible sites, human g.i. tract: 1424

NUCLEIC ACIDS, DNA

- alkylation, mechanism, review: 1011
- complex with benzpyrene, properties: 1088
- composition, adenovirus 12-induced hamster tumor: 1263
- content, bronchogenic carcinoma: 1426
- EB virus-infected Burkitt lymphoma cell lines: 1257
- effect of
 - aflatoxin, cell-free system: 1112
 - tumor cells: 1106
 - aryldialkyltriazenes, cell-free system: 1174
 - contraceptive hormones, human cervix: 1425
 - dimethylbenzanthracene, regenerating mouse liver: 1204
 - sex difference, rat mammary gland: 1069
 - hydroxylamine, bacteriophage: 1168
 - luteoskyrin, tumor cells: 1172
 - nitroso compounds, mechanism: 1150, 1151, 1155
- endonuclease, adenovirus-12 or -2-infected hamster or human cells: 1320
- Friend leukemia virus-infected mouse spleen: 1306
- Hodgkin's disease lymph node, induction of virus formation, HeLa cells: 1294
- methylcholanthrene + croton oil-induced skin tumors, mouse: 1054
- Rous sarcoma-Rous lymphoma virus-infected chick embryo cells: 1245
- SV40, properties: 1280, 1289, 1316
- synthesis, human cancer: 1420
- urethan-induced lymphoma, mouse: 1080

NUCLEIC ACIDS, RNA

- adenovirus group-specific, transformed cells: 1260
- aminoacyl-RNA synthetase, effect of benzanthrene and phenanthrene compounds, cell-free system: 1184
- effect of
 - aflatoxin, cell-free system: 1112
 - tumor cells: 1106
 - aryldialkyltriazenes, cell-free system: 1174
 - contraceptive hormones, human cervix: 1425
 - methylcholanthrene, rat liver: 1208
 - methylmethanesulfonate, rat liver: 1157
 - nickel carbonyl, rat liver: 1176
 - nitro or nitroso compounds, tumor cells or bacteria: 1146, 1151, 1155
- ethionine or α -naphthylisothiocyanate hepatoma, rat: 1173
- Friend leukemia virus-infected mouse spleen: 1306
- guinea pig tissues, effect on benzpyrene- or methylcholanthrene-induced mouse sarcomas: 1059
- Moloney sarcoma/leukemia virus-transformed rat cells (78A-1 line): 1246
- nucleolar (45S and 28S), composition, methyl-dimethylaminoazobenzene hepatoma, rat: 1143
- RNA-dependent RNA polymerase, viral avian myeloblastosis cells: 1230
- SV40, pathogenicity, hamster: 1316

NUCLEIC ACIDS, RNA, (Contd.)

- transformed cells: 1283
- synthesis, normal or neoplastic mouse liver: 1427
- transfer or ribosomal, methylation, carcinogen-induced hepatoma, rat: 1144
- transfer-RNA methylase, GA (Marek's disease-associated) virus-induced liver tumor, chick: 1319

NUCLEIC ACIDS, RNA, SYNTHETIC POLYMER (polyinosinic-polycytidylic acid)

- effect on Moloney or Friend virus-induced sarcoma, mouse: 1303

NUCLEOSIDES AND NUCLEOTIDES

- polynucleotides, effect of aflatoxin, cell-free system: 1112
- specific metabolic abnormalities, ethionine- or α -naphthylisothiocyanate-induced hepatoma, rat: 1173
- thymidine triphosphate, metabolism, methyl-dimethylaminoazobenzene liver tumors, rat: 1142

OCCUPATIONAL DISEASES

- aromatic amine exposure, bladder cancer, rubber industry, Britain: 1119
- asbestos exposure, pleural mesothelioma, West Germany (Hamburg): 1370
- chronic arsenic toxicity, Poland (Zloty Stok): 1118
- coal dust exposure, chronic bronchitis, smoking, Germany: 1117
- heavy metal exposure, cancer risk, review: 996
- radiation exposure, WBC chromosomes: 1030
- sinapylaldehyde exposure, nasopharynx cancer, review: 1004

OIL, ESSENTIAL

- citrus, effect on dibenzpyrene s.c. tumors, mouse: 1214

OIL, MINERAL (See also Petroleum)

- plasmacytoma
 - germ-free or conventional mice: 1175
- leukemia virus-like particles, mouse: 1250, 1251, 1298

OROPHARYNX NEOPLASMS

- epidemiology, U.S., environmental factors and ethnic groups: 1384

OVARY NEOPLASMS

- benign, lead acetate induction, rat: 1131
- homology to tumors of testis: 1383
- induction
 - dimethylbenzanthracene, mouse: 1074
 - methylcholanthrene, rabbit: 1047
- sex cord tumor, familial polyposis of colon (Peutz-Jeghers syndrome): 1403
- teratoma, spontaneous, mouse leukemia virus-containing, mouse: 1231

PARASITES

- Trichosomoides crassicauda, bladder infestation, effect on fluorenylacetamide bladder tumors, rat: 1171

PARATHYROID

- hyperplasia, incidence, strain differences, rat: 1433

ENIS NEOPLASMS

syphilis lesion: 1401

ERITONEAL NEOPLASMS

induction, plastics, rat: 1132

ERYLENE

biosynthesis, bacteria, effect of culture medium constituents: 1093

ESTICIDE SYNERGISTS

effect on benzpyrene metabolism, rat: 1095

ETROLEUM

processing plant, benzpyrene content of soil and vegetation, USSR: 1086

HENACETIN

kidney and bladder cancer, habitual abuse of analgesic preparation, Sweden: 1123

HENANTHRENE

metabolism, effect of methylcholanthrene, rat liver microsomes: 1049

HENANTHRENE DERIVATIVES

cysteine conjugates, effect on aminoacyl-RNA synthetase, cell-free system: 1184

HOSPHOLIPIDS

effect on methylcholanthrene tumors, mouse: 1064

liver, dimethylaminoazobenzene hepatoma, effect of riboflavin or antitumor anti-biotic, rat: 1139

HUTITARY NEOPLASMS

induction

estradiol valerate, mouse: 1129

lead acetate, rat: 1131

HANTS

benzpyrene content, soils near petroleum processing plant, USSR: 1086

ASMACYTOMA (See under myeloma and related diseases)

ASTICS

s.c. sarcoma, rat: 1132

AURA NEOPLASMS

mesothelioma

asbestos induction, rat: 1101

cultures, comparison with normal mesothelial cells: 1418

occupational asbestos exposure, West Germany (Hamburg): 1370

EGNANCY

reproductive histories

breast cancer, Massachusetts (Boston): 1356

Wales (southern): 1385

transplacental carcinogenesis

adenovirus-12, hamster: 1262

ethylnitrosourea, lung, mouse: 1152

nitroso compounds, brain, rat: 1191

rodent, review: 1005

Shope papilloma virus, skin, rat: 1327

OGESTATIONAL HORMONES

effect on dimethylbenzanthracene induction of cervix cancer, mouse: 1128

OSTATE

methylcholanthrene transformation in vitro, mouse: 1065

OSTATE NEOPLASMS

epidemiology, ethnic groups, Oklahoma: 1353

lead acetate induction, rat: 1131

methylcholanthrene-induced, hormone effects, rat: 1052

PROTEINS

albumin, effect on benzpyrene hydroxylase, rat liver microsomes: 1091

microsomal hemoproteins, effect of methylcholanthrene, rat liver: 1060, 1061, 1062

PROTEIN SYNTHESIS

effect of

aflatoxin, tumor cells: 1106

contraceptive hormones, human cervix: 1425

histidine decarboxylase inhibitors, rat tumors: 1243

methylnitrosourea or 2-deoxy-D-glucose derivative (streptozotocin), bacteria and tumor cells: 1155

steroid hormones, methylcholanthrene or cholesterol, human WBC: 1192

myeloma proteins, mouse myeloma cultures: 1428

polyribosomes, effect of tannic acid, rat liver: 1179

SV40-infected cells: 1286

PSYCHOLOGICAL FACTORS

psychosomatic aspects of cancer: 1411, 1412

PURINE N-OXIDES

s.c. tumors, structure-activity relationships, rat: 1189

PYRENE

metabolism, effect of methylcholanthrene, rat liver microsomes: 1049

PYRIDOXINE

effect on tryptophan metabolism, smokers: 1099

QUINAZOLINE, TRICYCLO-

epidermal hyperplasia, mouse skin: 1188

QUINOLINE, 0,0'-DIACETYL-4-HYDROXYAMINO-, 1-OXIDE

free radical formation and mechanism of action: 1165

QUINOLINIC ACID

excretion, dietary factors, Africa (Uganda): 1368

RADIATION

environmental light, effect on dimethyl-

benzanthracene mammary tumors, rat: 1041

occupational exposure, WBC chromosomes: 1030

sunlight

melanoma, Australia (Queensland): 1381

seasonal leukemia incidence, Poland

(Cracow): 1392

RADIATION CARCINOGENESIS

bone

Hiroshima and Nagasaki: 1027

rabbit: 1028

breast, pulmonary fluoroscopy, human: 1042

cervix uteri, tumor histology, mouse: 1036

corpus uteri, possible, human: 1037

connective tissue, rabbit: 1028

lung, tumor pathology, mouse: 1039

skin

rabbit: 1028

rat: 1038

RADIATION EFFECTS

chromosome breakage, plant: 1399

RADIATION EFFECTS, (Contd.)

- infectivity and tumorigenicity (hamster) of simian adenovirus SA-7: 1315
- leukemia incidence and kidney diseases, RF/Un mouse strain: 1040
- rescue of UV-irradiated SV40, transformed cells: 1288
- thyroid tumor promotion, human: 1029
- urethan lung carcinogenesis, mouse: 1081

RADIATION LEUKEMOGENESIS

- dog, ⁹⁰Sr: 1034
- human
 - ³²P, chromosomes: 1031
 - possible, Hodgkin's disease, chromosome abnormalities: 1405
- mouse
 - ⁶⁰Co, chromosomes: 1033
 - effect of sheep spleen or serum extracts: 1035
 - ³²P: 1228
 - virus-like particles: 1032
 - thymic lymphoma, possible leukemia virus: 1203

RADIOACTIVE ISOTOPES AND ELEMENTS

- ⁶⁰Co, leukemia, chromosomes, mouse: 1033
- ³²P, effect on WBC chromosomes, polycythemia vera: 1031
- mouse leukemia, pathology: 1228
- virus-like particles: 1032
- ²¹⁰Po, tobacco, smoking and lung cancer, review: 1024

RESERPINE

- effect on tryptophan metabolism, smokers: 1099

RESPIRATORY NEOPLASMS

- epidemiology, environmental temperature, geographical variations, U.S.: 1343
- upper respiratory tract and mouth cancer, smoking, U.S.: 1337

RETICULOENDOTHELIAL NEOPLASMS

- aberrations of group 17/18 chromosomes, review: 1015
- familial reticuloendotheliosis, SV40-transformation susceptibility of skin fibroblasts: 1225

RETICULOENDOTHELIAL SYSTEM

- WBC phagocytic activity, effect of carcinogens and related agents, rat: 1180

RIBOFLAVIN

- effect of liver phospholipids, dimethylamino-azobenzene hepatoma, rat: 1139

RUBBER

- dust, effect on tumor cells or tobacco callus *in vitro*: 1124
- occupational exposure, aromatic amine exposure, bladder cancer, Britain: 1119

SALIVARY GLAND NEOPLASMS

- induction
 - dimethylbenzanthracene
 - effect of cold stress, rat: 1072
 - strain difference, rat: 1073

SAPONIN(S)

- myelofibrosis with myeloid metaplasia, rabbit: 1163

SCAR TISSUE (See also under Injuries)

- alcoholic cirrhosis of liver, malignant transformation: 1415
- benign syphilis, penis cancer: 1401
- bone, sarcoma at site of injury, Paget's disease: 1404
- esophagus cancer, gastrectomy or gastroenterostomy: 1045
- lung, pathology of lung scar cancer, human: 1043, 1044

SEX DIFFERENCE

- cancer epidemiology, England/Wales and western Europe: 1389
- dimethylbenzanthracene effect on mammary gland DNA, rat: 1069
- skin tumors, effect of thymectomy, mouse: 1077
- esophagus cancer, South Africa (Transkei), ethnic groups: 1386
- thyroid tumor size, radiation effects, human: 1029

SINAPYLALDEHYDE (See Cinnamaldehyde, 3,5-dimethoxy-4-hydroxy-)

SKIN

- aflatoxin distribution, rat: 1108
- dermatoglyphic patterns, leukemia, Poland: 1391
- pre-malignant Bowen's disease, virus-like particles: 1295
- s.c. tissues, migration of asbestos fibers, mouse: 1103
- SKIN CARCINOGENESIS
 - aminofluorene and naphthalene derivatives, mouse: 1183
 - benzanthracene
 - cocarcinogen effects on threshold response, mouse: 1087
 - derivatives, mouse, structure-activity relationship: 1187
 - benzpyrene, mouse: 1078, 1087
 - bioassay of very weak carcinogens, new mouse strain: 1190
 - dimethylbenzanthracene
 - DOPA oxidase-positive melanocytes, mouse: 1067
 - effect of
 - orchiectomy, hamster cheek pouch: 1076
 - vinblastine or dimethyl sulfoxide, resistant mouse strain: 1079
 - mouse: 1078
 - tumor pathology, hamster cheek pouch: 1075
 - initial epidermal stages of 2-stage carcinogenesis, mouse: 1188
 - methylcholanthrene
 - amphibia (*Bufo arenarum*): 1056
 - cell growth kinetics, mouse: 1057
 - + croton oil, DNA and chromosomes, mouse: 1054
 - DOPA oxidase-positive melanocytes, mouse: 1067
 - effect of
 - growth hormone, mouse: 1055
 - of thalidomide, mouse: 1058
 - mouse: 1078
 - radiation, rabbit: 1028

IN CARCINOGENESIS, (Contd.)

rat: 1038
 Shope papilloma virus, fetal and adult rat: 1327
 tobacco smoke condensate, mouse: 1096, 1097, 1098
 s.c. tumors
 benzpyrene or methylcholanthrene, attempted induction, cattle: 1068
 dibenzpyrene, effect of essential oils, mouse: 1214
 hydroxyxanthine, mouse or rat: 1161
 methylcholanthrene
 effect of phospholipids or cholesterol, mouse: 1064
 host immunity, mouse: 1063
 nitroquinoline oxide-transformed embryonic cell cultures, rat: 1166
 plastics, rat: 1132
 purine N-oxides, structure-activity relationship, rat: 1189
 polyoma virus + fluorenylacetamide, synergism, rat: 1202
 radiation, rabbit: 1028
 urethan and related N-hydroxycarbamates, tumor initiation, mouse: 1186
 vitamin A palmitate, lymphoma-like tumors, hamster cheek pouch: 1164
 N NEOPLASMS
 differentiation of tumor stem cells, rat: 1421
 epidemiology
 age factors, Germany (Giessen): 1365
 India (Saurashtra): 1364
 melanoma, Australia (Queensland), geographical variations, sun exposure: 1381
 Minnesota: 1355
 genetic susceptibility or resistance, epidermal cell endoplasmic reticulum, mouse: 1422
 Kaposi's sarcoma, epidemiology, Nigeria: 1371
 malignant transformation of hidradenitis suppurativum: 1417
 neurofibromatosis, familial patterns of freckling: 1413
 benzpyrene content, petroleum processing plant, USSR: 1086
 FRIEND
 Graffi virus leukemia, pathogenesis, mouse: 1224
 nucleic acid and nuclease distribution, Friend leukemia virus-infected mouse: 1306
 pathology, polyoma virus-infected mouse: 1311
 OLON
 effect on
 Friend leukemia virus infection, role of interferon, mouse: 1321
 Moloney sarcoma or Friend leukemia virus in vitro: 1235
 T MACH NEOPLASMS
 epidemiology
 Colombia (Cali), ethnic groups, intestinal metaplasia: 1390
 dietary carcinogens, review: 1014

STOMACH NEOPLASMS, (Contd.)

proteins, international: 1432
 Poland (urban and nationwide): 1373, 1375
 risk of multiple primary tumors: 1359
 STREPTOZOTOCIN (See N-Nitrosourea, N-methyl-, 2-deoxy-D-glucose derivative)
 STRESS (See also under Injuries)
 cold, effect on dimethylbenzanthracene salivary gland tumors, rat: 1072
 crowding, effect on dimethylbenzanthracene mammary tumors, rat: 1070
 surgical trauma (mastectomy), effect on dimethylbenzanthracene mammary tumors, rat: 1071
 SV40 (See under Virus, papova)

TANNIC ACID

effect on protein synthesis, rat liver: 1179

TEMPERATURE

cold stress, effect on dimethylbenzanthracene salivary gland tumors, rat: 1072
 environmental, cancer mortality, geographical variations, U.S.: 1342, 1343

TESTIS NEOPLASMS

differentiation of tumor stem cells: 1421
 homology to tumors of ovary: 1383
 lead acetate induction, rat: 1131
 teratoma, spontaneous, mouse leukemia virus-containing, mouse: 1231
 pathology, mouse or rabbit: 1231
 Yaba poxvirus-induced, monkey, isolation and properties of virus: 1290

TESTOSTERONE

leiomyosarcoma of ductus deferens, autonomous hormone-independent lines, hamster: 1130

TESTOSTERONE PROPIONATE

effect on dimethylbenzanthracene induction of cervix cancer, mouse: 1128

THALIDOMIDE

effect on methylcholanthrene skin tumors, mouse: 1058

THYMUS

immunity, leukemogenesis, review: 991
 thymectomy
 effect on
 dimethylbenzanthracene skin tumors, sex difference, mouse: 1077
 host immunity, thymoma-bearing mice: 1198
 urethan lung tumors or lymphoma, mouse: 1083

THYMUS NEOPLASMS

dimethylbenzanthracene thymoma, host immunity, effect of thymectomy, mouse: 1198
 Graffi virus leukemia, pathogenesis, mouse: 1224

THYROID

human, cells, effect of SV40 infection: 1284
 methylcholanthrene-induced thyroiditis, pathology, rat: 1050

THYROID NEOPLASMS

epidemiology
 sex ratio, England/Wales and western Europe: 1389
 strain differences, rat: 1433

THYROID NEOPLASMS, (Contd.)

- lead acetate induction, rat: 1131
- sex difference in tumor size, radiation effects, human: 1029

TOBACCO SMOKE

- condensate
 - skin tumors (mouse): 1096
 - effect of curing methods: 1098
 - changes in tar/nicotine ratio: 1097
- filtered, abnormal growth patterns and chromosomes, mouse lung or kidney cells: 1211

TOBACCO SMOKING

- chronic bronchitis, coal miners, Germany: 1117
- lung cancer
 - and other tumors, U.S.: 1337
 - ²¹⁰Po content of tobacco, review: 1024
- tryptophan metabolism, effect of pyridoxine or reserpine, human: 1099
- urinary chemiluminescence, bladder cancer etiology: 1100

TOOTH

- odontogenic epithelium, polyoma virus transformation, mouse embryo: 1274

TOXICITY

- aflatoxin
 - amphibian larvae or chick embryo, bioassay method: 1109
 - skin-painted, rat: 1108
- cycasin and aglycone, germ-free or conventional rat, review: 995
- diethylnitrosamine, liver, fructose phosphate aldolase metabolism, rat: 1148
- dimethylbenzanthracene, mechanism, rat: 1210
- methylnitrosamines and methylnitrosamides, mouse: 1185

TRIAZENE COMPOUNDS

- 1-aryl-3,3-dialkyltriazenes, mechanism of action, cell-free system: 1174
- structure-activity relationship, rat: 1193

TRYPTOPHAN

- metabolism
 - bladder cancer: 1195
 - effect of pyridoxine or reserpine, smokers: 1099
 - tumor recurrence rate, bladder cancer: 1162

TRYPTOPHAN METABOLITES

- excretion, dietary factors, Africa (Uganda): 1368

URETHAN

- effect on polyoma virus-induced hemagglutinins, yeast: 1275
- epidermal hyperplasia, mouse skin: 1188
- lung tumors
 - effect of
 - butyl or isoamyl carbamate, mouse: 1082
 - cortisone, mouse: 1081
 - thymectomy, mouse: 1083
 - radiation effects, mouse: 1039, 1081
- lymphoma
 - effect of thymectomy, mouse: 1083
 - tumor cell DNA, mouse: 1080
- skin tumor initiation, mouse: 1186, 1188

URETHAN ANALOGS

- butyl or isoamyl carbamate, effect on urethan lung tumors, mouse: 1082
- N-hydroxycarbamates, skin tumor initiation, mouse: 1186

UTERUS NEOPLASMS (See Corpus uteri neoplasms)

VIRAL CARCINOGENESIS

- chromosomal abnormalities, classification, review: 1002
- hamster, parainfluenza-like viruses from British wild squirrels: 1299
- surface membrane properties, transformed cells: 1326
- transplantation antigens, animal and human, review: 1009

VIRUS

- foamy, latent infection, primate colony: 1276
- formation, HeLa cells exposed to DNA from Hodgkin's disease lymph node: 1294
- infection, autoimmunity, cancer pathogenesis, review: 1025
- intranuclear inclusion bodies, melanoma, human: 1292
- parainfluenza-like, isolation, (wild squirrels, Britain) and tumor induction (hamster): 1299
- particles resembling
 - Bowen's disease of skin: 1295
 - carcinogen-induced brain tumors, review: 992
 - methylcholanthrene-induced mouse brain tumor: 1297
- picodna (X-14 or H-1), multiplication, effect of polyoma virus, rat embryo cells: 1271
- RNA, particles resembling, human tumors: 1293

VIRUS, ADENO-

- human
 - group A, B or C, virus-specific RNA, transformed cells: 1260
 - oncogenic and non-oncogenic, plaque formation ability, calf kidney cell line: 1259

SA-7 (simian)

- hamster tumor, transplantability, effect of SA-7 immunization: 1308
- helper to human adenovirus-7, monkey kidney cells: 1329
- infectivity and tumor induction (hamster), effect of UV irradiation: 1315

SV30 (simian)

- effect on ultrastructure, monkey kidney cells: 1265

type 2

- DNA endonuclease, infected hamster or human cells: 1320
- virus-specific RNA, transformed cells: 1260

type 4

- SV40 hybrid, transformation (hamster cells) and tumor induction (hamster): 1267

type 7

- interaction with helper viruses (SV40 or simian adenovirus SA-7), monkey kidney cells: 1329

- VIRUS, ADENO- (Contd.)
 virus-specific RNA, transformed cells:
 1260
 type 12
 DNA endonuclease, infected hamster or human
 cells: 1320
 hamster tumors
 DNA composition: 1263
 effect of liver extract from clam:
 1310
 intracellular tumor antigen distribution:
 1266
 lipid composition: 1264
 Huie strain, transplacental tumor induc-
 tion, hamster: 1262
 virus-specific RNA, transformed cells:
 1260
 type 18
 serum antibodies, human cancer: 1261
 virus-specific RNA, transformed cells:
 1260
 type 31
 virus-specific RNA, transformed cells:
 1260
 VIRUS, HERPES
 infected hamster cells, surface Forssman
 antigen: 1325
 VIRUS, HERPES-TYPE
 Epstein-Barr (human)
 DNA synthesis, temperature effects,
 Burkitt lymphoma cell lines: 1257
 isolation, properties and distribution:
 1255
 serum antibodies, young adults, U.S.:
 1256
 isolation, guinea pig strain susceptible to
 L2C/NB leukemia: 1328
 Marek's disease (avian)
 associated GA virus, chick liver tumor,
 transfer RNA methylase: 1319
 infection, serum immunoglobulins, chicken:
 1258
 VIRUS, HYBRID
 adenovirus type 4-SV40, transformation,
 (hamster cells in vitro) and hamster tumor
 induction: 1267
 VIRUS, LEUKEMIA/LYMPHOMA
 AKR (mouse)
 tumor pathology: 1228
 avian
 cytotropism, review: 1012
 Rous lymphoma, Rous sarcoma virus replica-
 tion, DNA synthesis, chick embryo cells:
 1245
 BAI strain A (avian myeloblastosis)
 RNA-dependent RNA polymerase, cells: 1230
 334-C (mouse)
 effect on skin isograft survival, mouse:
 1227
 Friend (mouse)
 associated minimal-pathogenicity (Rowson-
 Parr) virus, isolation and properties:
 1215, 1216
 chloroma-inducing strain, pathogenicity,
 newborn mice: 1218
 effect of interferon inducer, cell culture:
 1235
 VIRUS, LEUKEMIA/LYMPHOMA, (Contd.)
 effect on skin isografts, mouse: 1227
 genetic susceptibility, bone marrow cells:
 1217
 infection, effect of interferon inducer,
 mouse: 1321
 intracellular nuclease and nucleic acid,
 mouse spleen: 1306
 Rowson-Parr variant, pathological and
 immunodepressive effects, mouse: 1216
 Graffi (mouse)
 pathogenicity, newborn mice: 1223, 1224
 Gross (mouse)
 intrathymic inj. and accelerated leukemia:
 1302
 particles resembling, radiation- or
 carcinogen-induced thymic lymphoma,
 mouse: 1203
 persistently-infected cell lines: 1309
 human
 mongolism with leukemia, review: 1026
 particles resembling, non-lymphomatous
 lymph node hyperplasia: 1233
 Moloney (mouse)
 Moloney sarcoma virus complex, transformed
 rat cells (78A-1), bicatenoid RNA:
 1246
 requirement as helper, Moloney sarcoma
 virus-infected mouse or rat cells:
 1247
 mouse
 Friend-Moloney-Rauscher complex, comparison
 to Parma leukemia virus: 1234
 infection, strain differences, mouse:
 1305
 occurrence, spontaneous ovarian or
 testicular teratomas, mouse: 1231
 Opler (guinea pig)
 pathology of lymphoblastic leukemia: 1226
 Parma (mouse)
 from Harvey sarcoma virus complex,
 properties: 1234
 radiation leukemia virus (mouse)
 particles resembling, radiation- or
 carcinogen-induced thymic lymphoma,
 mouse: 1203
 Rauscher (mouse)
 hamster tumor, properties of virus: 1220
 immunosuppression, mouse: 1219, 1318
 transformed rat embryo cells, properties:
 1221, 1222
 rodent
 cytotropism, review: 1012
 Type A particles
 ³²P-induced mouse leukemia: 1032
 Type C particles
 Bittner mouse mammary tumor virus-infected
 mouse cells: 1254
 mineral oil- or adjuvant-induced plasma-
 cytoma, mouse: 1250, 1251, 1298
 radiation-induced leukemia, mouse:
 1032, 1203
 VIRUS, MAMMARY TUMOR
 Bittner (mouse)
 infected mouse cells, release of leukemia
 virus particles: 1254

VIRUS, MAMMARY TUMOR, (Contd.)

mouse

- distribution and milk antigenicity: 1252
- high-MTV strain with low spontaneous mammary tumor incidence: 1253

VIRUS, PAPOVA (papilloma-polyoma-vacuolating)

bovine papilloma

- meningeal and brain tumors, calf: 1268
- transformation, cellular antigens, hamster or mouse embryo cells: 1270
- tumor pathology, cattle, horses and rodents: 1269

polyoma

effect on

- antigen production, yeast culture: 1275
- morphology, mouse spleen: 1311
- picodnavirus multiplication, rat embryo cells: 1271

- hamster sarcoma, transplantability: 1272
- membrane glycoproteins and glucosamines, transformed cells: 1324

- surface antigens, infected or transformed cells: 1273, 1324, 1325

- synergism with fluorenylacetamide, rat: 1202

- transformation, odontogenic epithelium, mouse embryo: 1274

Shope papilloma (rabbit)

- spontaneously regressing papillomas, rat: 1327

SV40

- adenovirus-4 hybrid, transformation (hamster cells) and tumor induction (hamster): 1267

- coat protein antigens, nonpermissive nuclei of heterokaryocyte cultures: 1277

- DNA, hybridization with cellular DNA, monkey cells: 1280

- effect on human thyroid cells: 1284

hamster tumors

- effect of heterologous or homologous nucleic acids: 1316

- pathology: 1281

- surface antigens: 1323

- helper to human adenovirus-7, monkey kidney cells: 1329

- infected cells, protein synthesis: 1286

- latent infection, epidemiology, primate colony: 1276

- monkey-mouse hybrid cell lines with viral genome: 1278

mutants

- isolation of double lysogens from transformed cells: 1279

- properties of DNA: 1289

transformation

- hamster cells: 1285

- relationship to tumorigenicity (hamster): 1282

- susceptibility, high-leukemia family: 1225

transformed cells

- human amnion cell lines: 1317

- membrane glycoproteins and glucosamines: 1287, 1324

- properties of RNA: 1283

VIRUS, PAPOVA, (Contd.)

- relationship of "crisis" to virus production, human cells: 1300
- surface antigens: 1322, 1323
- UV-irradiated, virus rescue: 1288

VIRUS, POX

Shope fibroma (rabbit)

- in vitro titration: 1291

Yaba histiocytoma (monkey)

- isolation (testis tumors of monkeys) and properties: 1290

VIRUS, SARCOMA

Finkel osteosarcoma (mouse)

- replication and transformation, rat embryo cells: 1314

Friend pseudotype (mouse)

- sarcoma, effect of synthetic RNA polymer, mouse: 1303

Harvey (mouse)

- properties of Parma leukemia virus from complex: 1234

- tumor cells, immunogenicity, mouse: 1248

Moloney (mouse)

defective

- properties, mouse or rat cells: 1247

- Rauscher leukemia virus from hamster tumor as helper: 1220

- effect of interferon inducer, cell culture: 1235

- infection and tumor development, kinetics, newborn mouse: 1304

- Moloney leukemia complex, transformed rat cells (78A-1), bicatenoid RNA: 1246

Moloney pseudotype (mouse)

- sarcoma induction, effect of synthetic RNA polymer: 1303

Rous (chicken)

Bryan strain

- infectivity, wild and domestic birds: 1239

- transformed hamster cells, virus-specific antigens: 1313

- hamster tumor (RHa), occurrence of virus particles: 1237

- monkey sarcoma, attempted virus unmasking: 1307

- rat tumors, effect of histidine decarboxylase inhibitors on protein synthesis: 1243

Schmidt-Ruppin strain

- brain tumors, dog: 1240

- hamster tumors, pathology: 1236

- virus isolation and pathogenicity, chick embryo: 1238

- infected chicken-mouse mixed cell cultures, tumor induction, mouse: 1241

- infectivity, wild and domestic birds: 1239

- mouse tumors, properties: 1242

rat tumors

- cellular and host immunity: 1244

- leukemoid reaction with sarcoma, germ-free rats: 1301

- pathology: 1236

- replication, Rous avian lymphoma-infected cells, DNA synthesis: 1245

SUBJECT INDEX

VIRUS, SARCOMA, (Contd.)

transformed marmoset kidney cells, tumor
induction, marmoset: 1312

ST fibrosarcoma (cat)

tumor induction, marmoset: 1249

VITAMIN A PALMITATE

effect on benzpyrene-induced lung and fore-
stomach tumors, hamster: 1089

lymphoma-like tumors, hamster cheek pouch:
1164

VITAMIN B2 (See Riboflavin)

VITAMIN B6 (See Pyridoxine)

XANTHINE, 3-HYDROXY-

s.c. tumors

mouse: 1161

rat: 1161, 1189

YABA VIRUS (See under Virus, pox)

ZINC

serum and tissues, lung and other cancer,
human: 1135

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Vet. Med.

AUGUST 1970

Abstract Nos. 1436-1710

Vol. 8

No. 8

CARCINOGENESIS ABSTRACTS

National Cancer Institute

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE • National Institutes of Health

CARCINOGENESIS ABSTRACTS

Volume 8, Issue 8

Abstract Numbers
1436-1710

CONTENTS

	<u>Page</u>
Review	279
Physical Carcinogenesis	281
Chemical Carcinogenesis	283
Viral Carcinogenesis	299
Epidemiology and Biometry	312
Miscellaneous	323
Author Index	i
Subject Index	v

Prepared by Scientific Literature Corporation
Philadelphia, Pennsylvania 19103

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Persuant to a Contract with the Public Health Service
U.S. Department of Health, Education and Welfare
PH43-70-2036

Use of funds for printing this publication approved
by the Director of the Bureau of the Budget on July 25, 1967.

The National Cancer Institute, in response to Congressional interest and desire for a national program of cooperative research in cancer, is establishing a means whereby information in the field of carcinogenesis will be coordinated and made available. The information to be included will be obtained from the National Cancer Institute, other governmental agencies, and non-governmental research institutions.

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NOTE

Journal names are abbreviated according to the list of abbreviations used by Index Medicus. If the journal is not covered by Index Medicus, then the abbreviations (with some modifications) found in World Medical Periodicals, 3rd Edition, are used.

ABBREVIATIONS USED IN ABSTRACTS

admin.	administered, administration	mg	milligram(s)
av.	average	min.	minute(s)
C	curie(s)	ml	milliliter(s)
mC	millicurie(s)	mm	millimeter(s)
μC	microcurie(s)	mo.	month(s)
cm	centimeter(s)	MTD	maximum tolerated dose
conc.	concentration	NIH	National Institutes of Health, USA
cpm	counts per minute	p.o.	orally
DNA	deoxyribonucleic acid	QO2	oxygen quotient
DNase	deoxyribonuclease	PFU	plaque forming unit
e.g.	for example	ppm	parts per million
FFU	focus forming unit	pt.(s)	patient(s)
g.i.	gastrointestinal	RBC	red blood cells (erythrocytes)
g	gram(s)	RES	reticuloendothelial system
μg	microgram(s)	resp.	respectively
Hb	hemoglobin	RNA	ribonucleic acid
i.a.	intra-arterial	RNase	ribonuclease
D50	median infectious dose	soln.	solution
inj.	injected, injection(s)	s.c.	subcutaneous
inoc.	inoculated, inoculation(s)	TCID	tissue culture infectious dose
i.p.	intraperitoneal	x	times (e.g. x 3/wk.)
i.u.	international unit(s)	U	unit
i.v.	intravenous	UV	ultraviolet
kg	kilogram(s)	vol.	volume
D50	median lethal dose	VA	Veterans Administration
M	molar, mole(s)	wt.	weight
mM	millimole(s)	WBC	white blood cells (leukocytes) or white blood cell count
μM	micromole(s)		
max.	maximum	yr.	year(s)

LANGUAGE ABBREVIATIONS

f.	Afrikaans	E.	English	Hun.	Hungarian	Lith.	Lithuanian	Ser.	Serbo-Croatian
r.	Arabic	Eston.	Estonian	lc.	Icelandic	Maced.	Macedonian	Sl.	Slovene
ul.	Bulgarian	Fin.	Finnish	In.	Indonesian	Nor.	Norwegian	Sp.	Spanish
h.	Chinese	Fr.	French	It.	Italian	Pol.	Polish	Sw.	Swedish
z.	Czech	Ger.	German	Jap.	Japanese	Por.	Portuguese	Th.	Thai
an.	Danish	Gr.	Greek	Kor.	Korean	Rum.	Rumanian	Uk.	Ukrainian
ut.	Dutch	Heb.	Hebrew	Latv.	Latvian	Rus.	Russian	Viet.	Vietnamese

70-1436 CANCER AND ENDOGENOUS FACTORS. (Fr.) Mathé, G. (Paul-Brousse Hosp. Inst. Cancer, Villejuif, France). Rev. Path. Comp. Med. Exp. 69(6):161-167, 1969. (79 references)

A summary of congenital, genetic and immunological factors which favor the development of human and experimental cancers is presented.

70-1437 GENETIC AND IMMUNOLOGIC FACTORS IN HUMAN LEUKEMOGENESIS. (Fr.) Degos, L. (St. Louis Hosp., Paris) and J. Dausset. Sem. Hop. Paris 46(5):309-317, 1970. (126 references)

It is concluded that leukemogenesis may depend upon a combination of weak defense mechanisms of the pt. and relative similarity between the antigens of the viral envelope and those of the host cell membrane.

70-1438 CYTOCHEMICAL ASPECTS OF LEUKEMIA AND LYMPHOMA. (E.) Hayhoe, F. G. J. (U. Cambridge, England). Seminars Hemat. 6(3):261-270, 1969. (32 references)

The significance of cytochemical findings (enzymes, DNA and RNA) in the pathogenesis of human leukemias is discussed.

70-1439 CARCINOGENESIS BY CHEMICALS: AN OVERVIEW - G. H. A. CLOWES MEMORIAL LECTURE. (E.) Miller, J. A. (U. Wisconsin Med. Ctr. McArdle Lab. Cancer Res., Madison). Cancer Res. 30(3):559-576, 1970. (175 references)

The role of chemicals, such as aromatic amines and amides and their esters, in carcinogenesis is discussed. It is suggested that the ultimate chemical carcinogens are strong electrophilic reactants.

70-1440 INVESTIGATIONS ON THE N-HYDROXYLATION OF AROMATIC AMINES AND ITS SIGNIFICANCE IN THE GENESIS OF URINARY BLADDER TUMORS. (Ger.) Lehleke, H. (U. Tübingen Pharmacol. Inst., Germany). Arzneimittelforschung 19(7):1033-1039, 1969. (78 references)

The metabolism of arylamines, carcinogenic activity of metabolites, resorption of arylhydroxylamines from the bladder and *in vitro* and *in vivo* studies on N-hydroxylation of various arylamines are reviewed. In contrast to N-hydroxylation of 4-aminobiphenyl and of β -naphthylamine by liver microsomes, N-hydroxylation of α -naphthylamine does not occur *in vitro*. Stimulation of hydroxylation and of carcinogenic activity by pretreatment with different substances is described, and the significance of

different possible reactions of metabolites with cellular components, in relation to carcinogenesis, is discussed.

70-1441 ISONIAZID AND CARCINOGENESIS. (Fr.) Lesobre, R. (Beaujon Hosp., Cligny, France), J. Ruffino and M. Tubiana. Sem. Hop. Paris 45(43):2657-2661, 1969. (23 references)

It is concluded that there is no evidence that isoniazid is a lung carcinogen in man, although it appears to be so in certain strains of experimental mice.

70-1442 TUMOR SPECIFIC TRANSPLANTATION ANTIGEN. (E.) Koldovský, P. (Wistar Inst., Philadelphia, Pa.). Rec. Results Cancer Res. 22:1-75, 1969. (322 references)

The role of tumor-specific transplantation antigen in cancer is presented. Among the important topics discussed are characteristics of the antigen, immunity and carcinogenesis, virus-induced tumors, chemical carcinogens, methods of detection of antitumor immunity, chorioepithelioma, tumor growth and development of immunity.

70-1443 THE RELATION BETWEEN THE EPSTEIN-BARR VIRUS AND INFECTIOUS MONONUCLEOSIS, BURKITT'S LYMPHOMA AND CANCER OF THE POSTNASAL SPACE. (E.) Henle, W. (U. Pennsylvania Sch. Med., Philadelphia) and G. Henle. E. Afr. Med. J. 46(7):402-405, 1969. (16 references)

Data regarding Burkitt's lymphoma (BL) were discussed at the International Agency for Research on Cancer at Nairobi in December, 1969. The climatic and age distribution, the multifocal onset, and clustering of pts. in several regions was related to an infectious etiology. A herpes-like virus (the Epstein-Barr virus) was proposed as a possible etiologic agent; because of its world-wide distribution, a relationship to other diseases, such as infectious mononucleosis, was considered.

70-1444 CANCER PREVENTION AND COMPETITIVE RISKS. (E.) Hammond, E. C. (Amer. Cancer Soc., Inc., New York, N. Y.). Arch. Environ. Health (Chicago) 19(3):395-402, 1969. (18 references)

Methods of currently available cancer control, cancer prevention, and competitive risks involved for cancer and other important diseases are discussed.

70-1445 EARLY DETECTION OF CANCER. REPORT OF A WHO EXPERT COMMITTEE. (E.) WHO

Expert Committee on Early Detection of Cancer (Geneva, Switzerland). WHO Techn. Rep. Ser. 422:1-35, 1969. (29 references)

The early detection of cancer is discussed extensively, based on a technical report of a World Health Organization Expert Committee presented at Geneva, Switzerland in November, 1968. Consideration is given to the objectives of cancer detection; screening tests, organization and evaluation of early detection programs, education and training.

70-1446 CANCER AND THE AGING PROCESS. (It.) Gavosto, F. (U. Turin Inst. Gen. Clin. Med., Italy), P. Masera and G. Rovera. G. Geront. Suppl. 40(Pt. 2):5-30, 1969. (151 references)

It is concluded that the aging process is accompanied by increasingly inadequate function of the mechanisms which result in elimination of defective or transformed cells before clones can develop. This appears to account for the demonstrable bilogarithmic correlation between aging and increased incidence of tumors.

70-1447 FAMILIAL LEUKEMIAS. (Fr.) Fournier, A. (St. Antoine Hosp. Pediat. Med. Clin., Lille, France), J. Huguet, A. Pauli, J. Cousin and M. Rollet. Sem. Hop. Paris 46(2): 87-100, 1970. (209 references)

Two cases of familial leukemia are included in an extensive review. One pt., a 4-yr.-old girl, died of acute lymphoblastic leukemia nearly 5 yr. after a sister developed the same disorder when about the same age. The second case involved monozygotic female twins (of a set of fraternal triplets), who developed acute lymphoblastic leukemia 2 mo. apart, and died at the ages of 7 or 13 mo. The other triplet (a male) remained in good health at the age of 4.5 yr.

70-1448 CANCER IN THE TROPICS. A COMPARATIVE STUDY WITH SPECIAL REFERENCE TO INDIA. (E.) Jussawalla, D. J. (Tata Mem. Hosp., Parel, Bombay, India) and S. K. Bhansali. Indian J. Cancer 6(1):1-26, 1969. (153 references)

Various forms of cancer found in tropical lands are presented, with special emphasis on India. Carcinoma of the oral cavity and pharynx, gastrointestinal tract below the hypopharynx (esophagus, liver, rectum and anal canal), genital tract, breast, urinary bladder, skin, lung, and leukemias and lymphomas, are discussed. Data from at least 15 countries are given for comparison, and the relationship of several cancers to local habits and customs, and inter-religious differences, are mentioned.

70-1449 POLYPS OF THE LARGE BOWEL AND URINARY BLADDER. (E.) Kelley, N. R. Trans. Ass. Life Insur. Med. Dir. Amer. 52:179-195, 1969. (27 references)

The risks of cancer development in pts. with polyps of the colon and rectum (excluding familial polyposis) and papillomas of the urinary bladder are discussed, from the viewpoint of the insurance underwriter.

70-1450 CELL PROLIFERATION DURING CARCINOGENESIS. (E.) Reiskin, A. B. (Argonne Nat. Lab., Ill.). Rec. Results Cancer Res. 17: 128-135, 1969. (47 references)

The kinetics of DNA synthesis and cellular division in neoplastic transformation *in vivo* and *in vitro*, including factors specific for given carcinogens and tissues, are discussed.

70-1451 DOUBLING TIMES OF BRONCHOGENIC CANCERS. (Fr.) Israel, L. (Cochin Hosp., Paris) and P. Chahinian. Rev. Franc. Etud. Clin. Biol. 14(7):703-710, 1969. (55 references)

It is concluded that human tumors continue to grow exponentially throughout their entire development, even though experimental tumors do not. This, in turn, implies that a considerable time is necessary for the development of metastasis, prior to detection of bronchogenic tumors, and that surgical intervention should always be accompanied by prolonged, intensive chemotherapy.

See also abstract no.: 1704

70-1452 CONDITIONS FOR THE DEVELOPMENT OF RADIATION CANCER (REPORT OF 39 CASES). (Rus.) Kozlova, A. V. (Sci. Res. Inst. Roentgen.-Path., Moscow). Med. Radiol. (Moskva) 14(5): 3-12, 1969.

Radiation-induced cancers (mostly squamous cell or basal cell carcinomas, with at least 1 case each of angiosarcoma, fibrosarcoma and osteogenic sarcoma), seen in 39 pts., were usually multiple. In 12 radiologists and radiation technicians, exposed to total radiation doses of 3500-32,500 r from age 21-32 yr. to age 55-60 yr., the latent periods were 20-30 yr. after the first radiation exposure. The development of cancer was preceded by atrophy and ulceration of the irradiated areas (thumb and dorsal surface of the wrist). Skin atrophy usually developed after 11-17 yr. of radiation exposure, but this latent period was only 3-7 yr. in pts. who had also been exposed to chemical irritants. One pt. died with metastases and 2 others died with cancer of the esophagus (1) or uterus (1), after 7-11 yr. of observation; the other 9/12 were alive without recurrences after 8-10 yr. These occupational radiation cancers, by comparison to the tumors observed in 27 pts. previously admin. radiotherapy (RT) for other diseases, were relatively late, slowly-growing and benign. In 10 pts. admin. RT (450-550 r x 1) for trichophytosis, the latent periods (16-41 yr.) varied according to the age at RT (5-15 yr.). In 9 pts. admin. RT (750-10,000 r in 3-20 courses over 1-21 yr.) for eczema, the latent periods (14-46 yr.) varied according to the RT dosage. These pts. had developed radiation dermatitis before the onset of cancer. The other 8 pts. had received RT (1600-12,000 r in 1-12 courses over 4 weeks-6 yr.) for malignant tumors; 5 pts. with histories of radiation dermatitis later developed single tumors, while 3 pts. without radiation dermatitis developed multiple tumors. Latent periods in these 8 pts. were 3-22 yr. Many pts. in the last 3 groups died with recurrent and/or metastatic radiation-induced cancer.

70-1453 ^{90}Sr IN OSSEOUS TISSUE IN THE POPULATION OF THE USSR (1957-1967). (Rus.) Gerasimov, A. N., B. K. Borisov and R. M. Barkhudarov. Ig. Sanit. 34(3):37-43, 1969.

Samples of bone (from 3445 cadavers) and teeth (from about 114,000 persons), obtained from 7,270 inhabitants of the USSR in 1957-1967 (inclusive), were analyzed for ^{90}Sr levels. An increase in osseous ^{90}Sr was seen during 1963-1966, with a marked decrease thereafter. The conc. of ^{90}Sr in the body in men varied according to age and residential locality. In similar population groups, the distribution of osseous ^{90}Sr levels followed a log normal pattern. The ratio of skeletal ^{90}Sr to the calcium content of the mothers' diet was 0.05 in newborn infants.

The ratio of skeletal ^{90}Sr to dietary calcium was 0.16 in children aged 1-3 yr. and 0.02 in adults (20 and over). In children up to 4 yr. of age, the highest osseous ^{90}Sr levels were seen in 1963-1964, corresponding to the period of max. ^{90}Sr levels in milk. In the 14-19-yr. age group, the corresponding peak was seen in 1965 (with a decrease of about 60% as of 1967). In a series of specimens obtained from Moscow, the highest ^{90}Sr conc. was noted in 1966, with a tendency to decrease in 1967. Av. ^{90}Sr levels (in $\mu\text{C}/1\text{ g}$ calcium) in osseous specimens obtained from infants (aged 0-1 yr.) in 1963-1965 were 4.60-5.40 in the USSR and 4.95-5.93 in Moscow, compared to 5.2-8.6 in England, 4.2-6.5 in Denmark, 6.9-15.0 in Norway and 5.0-7.9 in New York. The highest integral lifetime ^{90}Sr dose load was seen in persons born during the period of the most intensive nuclear weapons testing. In adults showing the highest ^{90}Sr levels, the absolute value of the av. annual ^{90}Sr dosage in osseous tissues did not exceed 10% of the threshold dosage established as permissible in the USSR.

70-1454 CYTOGENETICS OF MURINE LEUKEMIAS. (Sp.) Stockert, J. C. (Nat. Acad. Med. Inst. Hemat. Res., Buenos Aires, Argentina) and E. A. D. Holmberg. Medicina (B. Air.) 28(Suppl. 1):125-132, 1968.

A mean chromosomal number of 40 was found in 11/14 mice bearing a primary ^{32}P -induced leukemia; in 2/14, cells were hyperdiploid; in 1/14, hypertetraploid. The percentage incidence of aneuploidy was increased considerably, as compared to non-leukemic mice of the same strain. Extra chromosomes were large in some instances, very small in others. In mice bearing a cellular transplant of the same leukemia, 42 chromosomes were usually seen, 1 of the extras being a characteristic, very short, marker chromosome found in 50%-75% of the cells. In mice bearing a leukemia induced by inoc. of cells from a Burkitt's lymphoma cultivated *in vitro*, leukemic cells also showed 42 chromosomes, one of the extras being a large marker chromosome appearing to belong to group 2 and found in 50%-66% of the cells. Some 20% of the metaphases were tetraploid. Mouse leukemia induced by inoc. of biopsy material from a pt. with Hodgkin's disease was characterized by cells with 40 chromosomes and the presence of an extremely long marker chromosome in 80% of the cells. It is concluded that the leukemogenic effect of ^{32}P could not be correlated with the cytogenic changes it induced, and that the chromosomal constitution in mice with leukemias induced by human material excluded the possibility of colonization of human cells *in vivo*.

70-1455 THE EFFECT OF LONG-TERM USE OF IUD.
(E.) Hata, Y. (Iwate Med. U., Morioka, Japan), A. Ishihama, N. Kudo, Y. Nakamura, T. Miyai, T. Makino and T. Kagabu. Acta Obstet. Gynec. Jap. 16(2):73-78, 1969.

Through the end of October, 1967, 1075 Japanese women who were wearing, or had worn, intrauterine contraceptive devices (IUD) during 1952-1967 were followed up. In 1058 IUD wearers and 7226 control women, the frequencies of Class I, II or III cervical smears were the same. No Class IV or V smears were found among the IUD wearers. Class IV and V smears were seen in 0.2% and 0.01%, resp., of the controls, and 14 controls showed early cancers (including carcinoma *in situ*) of the cervix. Endometrial biopsies showed a slightly higher frequency of inflammatory changes among 518 IUD wearers than among 74 controls; no endometrial cancers were found in either group. The duration of IUD use (up to 16 yr.; 0-5 yr. in most women) was not correlated to the degree of cytological change observed in the cervix or endometrium. It is concluded that the use of IUD, even for prolonged periods, has no long-term adverse effect.

70-1456 PRIMARY ADENOCARCINOMA OF THE VAGINA FOLLOWING THE USE OF A PESSARY. (Fr.) Lamotte, G. (St. Elizabeth Obstet. Clin., Namur, Belgium). Bull. Soc. Roy. Belg. Gynec. Obstet. 39(4):287-294, 1969.

Following some 13 yr. use of a rubber pessary, inserted and withdrawn by the pt. without medical supervision, a 67-yr.-old woman with a first-degree prolapse of the uterus presented with a primary, ulcerative adenocarcinoma of the vagina, which was confirmed by biopsy.

70-1457 CARCINOMA OF THE ESOPHAGUS AT THE SITE OF LYE STRICTURE. (E.) Lansing, P. B., W. A. Ferrante and J. L. Ochsner (Alton Ochsner Med. Found., New Orleans, La.). Amer. J. Surg. 118(1):108-111, 1969.

A 54-yr.-old woman, who had swallowed a lye soln. 22 yr. previously, was examined because of increasing difficulty in swallowing of 6 mo. duration. In the past, but no longer, inter-

mittent dysphagia had been relieved by esophageal dilatation. Biopsy and esophagoscopy did not show a definite tumor, but surgical exploration showed a well-differentiated squamous cell carcinoma, not invading the muscularis. The prognosis was considered much better for esophageal cancer in these cases, because the dense scar tissue can prevent early neoplastic invasion.

70-1458 CANCER ARISING IN BURNED AREAS. (Fr.) Kayabali, I. and M. Duman (3rd Surg. Clin., Ankara, Turkey). Lyon. Chir. 66(1): 29-33. 1970.

The incidence, histology, pathology, prognosis and treatment of cancers arising in burn scar tissue in 18 men and 6 women (25-64-yr.-old, all with squamous cell carcinomas) are presented. It is concluded that the mechanisms involved in producing such cancers are still unknown, although the widespread use of proprietary ointments containing coal tar derivatives for treating pruritus or chronic ulceration of the scar tissue may be implicated in some cases.

70-1459 X-RAY AND X-RAY-PLUS-URETHANE INDUCTION OF "LEUKEMOGENIC" ACTIVITY IN TISSUES OF MICE: PRELIMINARY ELECTRON MICROSCOPIC STUDIES. (E.) Brown, R. C. (Oak Ridge Nat. Lab., Tenn.), V. Covelli, A. C. Upton and L. C. Satterfield. Proc. Amer. Ass. Cancer Res. 10:10, 1969.

70-1460 MYELOID LEUKEMIA IN HODGKIN'S DISEASE (HD); CHROMOSOMAL STUDIES. (E.) Ezdinli, E. Z. (Roosevelt Park Mem. Hosp., Buffalo, N. Y.), A. A. Sandberg and J. E. Sokal. Proc. Amer. Ass. Cancer Res. 10:23, 1969.

70-1461 FURTHER STUDIES ON THE COMPARATIVE EFFECTS OF DIET ON INCIDENCE OF TUMORS IN MICE EXPOSED TO MULTIPLE SUBLETHAL DOSES OF TOTAL BODY X-IRRADIATION. (E.) Field, J. B. (U. Southern California, Los Angeles), G. S. Bajwa, L. A. Bavetta and B. H. Ershoff. Proc. Amer. Ass. Cancer Res. 10:25, 1969.

See also abstract nos.: 1475, 1508, 1672, 1705

70-1462 IN VITRO EFFECTS OF CHEMICAL CARCINOGENS. (E.) Flaks, A. (Leeds Sch. Med., England) and J. M. Hamilton. Europ. J. Cancer 6(2):151-153, 1970.

Pulmonary explants derived from 1-mo.-old inbred BALB/c female mice were maintained *in vitro* for 2 days in a medium containing 3-methylcholanthrene (MC; 4 µg/ml), isoniazid (INH; 200 µg/ml), urethan (U; 200 µg/ml) or N-2-fluorenylacetamide (FAA; 10 µg/ml). Explants were then implanted s.c. into adult BALB/c mice, and the implants were studied at 3-mo. intervals for 1 yr. MC alone was active in a direct manner, inducing adenomatous and adenocarcinomatous lesions. INH, U and FAA, which require activation *in vivo*, did not induce neoplastic lesions. It is concluded that this *in vitro* culture method may be useful in studies of the mechanisms of action of chemical carcinogens.

70-1463 PROPOSED EXPERIMENTAL METHOD FOR USING MICE TO EVALUATE THE POTENTIAL CARCINOGENIC EFFECTS OF DRUGS. (It.) Cioli, V. (A. C. R. Pharmacol. Lab., Rome), P. S. Barcellona and B. Silvestrini. Boll. Soc. Ital. Biol. Sper. 45(13):857-860, 1969.

Cutaneous tumors developed in 56.43% of 2-mo.-old Swiss mice treated with 3-methylcholanthrene (0.5% soln. in acetone + chloroform; 6 topical applications over 3 weeks) and in 17.58% of those treated with urethan (10% soln. in acetone; 3 topical applications over 18 days) + croton oil (0.5% soln. in acetone; 1 dose/week x 18 weeks). No tumors developed in animals treated (as above) with urethan or croton oil alone, with a 10% soln. of a proprietary antiphlogistic called "Bendazac", or with the "Bendazac" soln. + croton oil (or + urethan).

70-1464 GASTRO-INTESTINAL TUMOURS IN RATS AND MICE FOLLOWING VARIOUS ROUTES OF ADMINISTRATION OF N-METHYL-N-NITROSO-N'-NITROGUANIDINE AND N-ETHYL-N-NITROSO-N'-NITROGUANIDINE. (E.) Schoental, R. (Med. Res. Council, Carshalton, Surrey, England) and J. P. M. Bensted. Brit. J. Cancer 23(4):757-764, 1969.

N-Methyl-N-nitroso-N'-nitroguanidine (MNG) or N-ethyl-N-nitroso-N'-nitroguanidine (ENG) were admin. i.p. or intragastrically (in various doses and dose schedules) to adult white rats and 1-2-mo.-old male C3H and CFW mice. In rats admin. MNG, i.p. admin. favored the development of intestinal tumors, while intragastric admin. favored the development of gastric tumors; a less marked response occurred for ENG admin. in rats. No g.i. tumors emerged in mice receiving either i.p. or intragastric ENG, although some tumors did develop after admin. of MNG.

70-1465 THE EFFECT OF LIMITED ADMINISTRATION OF N-METHYL-N'-NITRO-N-NITROSOGUANIDINE ON THE INDUCTION OF STOMACH CANCER IN RATS. (E.) Fujimura, S. (Nat. Cancer Ctr. Res. Inst., Chuo-ku, Tokyo), K. Kogure, T. Sugimura and S. Takayama. Cancer Res. 30(3):842-848, 1970.

In male Wistar rats, admin. of N-methyl-N'-nitro-N-nitrosoguanidine (NG; 83 or 167 µg/ml soln. x 7 mo., followed by tap water x 3-6 mo.) induced more adenocarcinomas of the glandular stomach than continuous admin. of NG (167 µg/ml soln.) for 1 yr. or more. Tumors of the forestomach, small intestine or mesentery were induced by continuous NG admin. or a higher conc. for 7 mo.

70-1466 DERMAL COLLAGEN CHANGES DURING 2-AMINO-ANTHRACENE CARCINOGENESIS IN THE RAT. (E.) Pinto, J. S. (U. Oregon Med. Sch., Portland), R. L. Dobson and J. P. Bentley. Cancer Res. 30(4):1168-1173, 1970.

In young Sprague-Dawley rats treated topically with 2-aminoanthracene (AA; 1% soln.; 2 admin./week x 14 weeks), a significant depression of collagen synthesis localized to the AA-painted site occurred. This response was independent of inflammation and growth rate, and collagen aggregation and breakdown were not influenced by AA treatment. The significance of these findings for epithelio-mesenchymal interactions and epidermal carcinogenesis is discussed.

70-1467 p-HYDROXYPROPIOPHENONE EFFECTS ON AZO DYE-INDUCED ALTERATIONS IN MOUSE HEPATIC CELLS: LIGHT AND ELECTRON MICROSCOPIC STUDY. (E.) Unakar, N. J. (Oakland U., Rochester, Mich.). J. Nat. Cancer Inst. 44(4):873-891, 1970.

Strain BUB mice received long-term exposure to dimethylaminoazobenzene (DAB; 0.06% in diet) or DAB + p-hydroxypropiophenone (PHP; 1%). Disruption of hepatic cords and hepatocytes, and a less than normal reaction for glycogen were noted after 3 weeks of DAB admin.; after 9 weeks, several small nodules were seen. Ultrastructural alterations in liver cells (after 3 weeks) included partial segregation of nucleolar content, an increased number of free ribosomes, peripheralization of chromatin material, increased branching tubular network of smooth endoplasmic reticulum, disorganization and apparent reduction of rough endoplasmic reticulum profiles, and increased electron density of mitochondrial matrix. These changes were greater after 6-9 weeks of DAB feeding, but the number of cells decreased on prolonged DAB admin. and alterations were less severe in altered cells. Cells of mice fed DAB + PMP had only slight initial changes after 3 weeks, and

although its mode of action is unknown, PHP apparently inhibited DAB-induced alterations in mouse liver cells.

70-1468 IRREVERSIBLE FIXATION OF INCREASED LEVEL OF MUSCLE TYPE ALDOLASE ACTIVITY APPEARING IN RAT LIVER IN THE EARLY STAGE OF HEPATOCARCINOGENESIS. (E.) Endo, H. (Kyushu U., Cancer Res. Inst. Fukuoka, Japan), M. Eguchi and S. Yanagi. Cancer Res. 30(3):743-752, 1970.

Adult Wistar rats were admin. 3'-methyl-4-dimethyl-aminoazobenzene (MeDAB; 0.06%, for 15, 30, 45 or 60 days) and the muscle-type aldolase (mtA) activity in the liver was determined. In comparison to normal liver, mtA was elevated, but the total aldolase activity, histological structure, mitotic index, soluble protein and DNA content showed no appreciable differences. Enzymatic change was evident after 15 days of MeDAB admin.; increased mtA activity in the liver of rats fed MeDAB for 60 days was maintained as long as 300 days. Results for N,N'-2,7-fluorenylenebisacetamide were similar, but the noncarcinogen, 2-methyl-4-dimethylaminoazobenzene, did not induce enzymatic change.

70-1469 DISTRIBUTION OF INTRAVENOUSLY INDUCED METASTASES IN HEPARIN- AND COUMARIN-TREATED MICE. (E.) Hagmar, B. (U. Goteborg, Sweden) and B. Boeryd. Path. Europ. 4(2):103-111, 1969.

Metastases in 2 syngeneic tumor-host systems, a 3-methylcholanthrene-induced rhabdomyosarcoma (MCG1-SS) in inbred CBA mice and melanoma B16 in C57BL/6J mice, were studied for the effects of heparin (1 mg in 0.02 ml soln. every 8 hours x 6 days) and phenprocoumon (0.02 mg in 0.04 ml soln. i.p., 1 admin./day, and 0.02 ml saline s.c., 2 admin./day x 6). Heparin decreased the mass of pulmonary metastases in both systems, without significantly changing extrapulmonary forms. Phenprocoumon increased the number and total vol. of B16 metastases in the lungs and of MCG1-SS metastases in some extrapulmonary organs. It is concluded that thrombus formation inhibits, rather than promotes, the establishment of metastases. The fact that heparin probably affects formation of lung metastases by mechanisms other than inhibited blood coagulation is discussed.

70-1470 CARCINOGENIC EFFECT OF PHENANTHROTHIAZOLES. (Rus.) Linnik, A. B. (Inst. Exp. Clin. Oncol., Moscow) and N. I. Golub. Vop. Onkol. 15(8):54-57, 1969.

In (C57 x CBA)F₁ hybrid mice (both sexes), topical applications of an 0.5-0.75% acetone soln. of phenanthro(2,1-d)thiazole (2 applications/week x 13 weeks, total about 10 mg) induced benign papillomas of the skin in only 2/33 of the 19-mo. survivors. Similar applications

of 2-methylphenanthro(2,1-d)thiazole (total 20 mg in 31 weeks) induced 1 benign papilloma and 35 malignant tumors, the first of which appeared after 9 mo. of observation. Tumors were found in 31/33 and 10/10 mice surviving 12 and 18 mo., resp. One small cell sarcoma was found; the other tumors were keratotic squamous cell carcinomas, often metastasizing to the lungs. These tumors were readily transplantable by s.c. inoc. (the tumor take rate was 80%) and many mice with transplanted tumors developed lung metastases. After 6 transplant generations, these tumors remained histologically unchanged.

70-1471 RNA SYNTHESIS INDUCTION IN CELL CULTURE BY A TUMOR PROMOTER. (E.) Sivak, A. (New York U. Med. Ctr. Inst. Environ. Med., N. Y.) and B. L. Van Duuren. Cancer Res. 30(4):1203-1205, 1970.

Phorbol myristate acetate (PMA; 0.5 µg/ml) enhanced RNA synthesis in stationary cultures of 3T3 mouse fibroblasts, leading to a release of density-dependent inhibition of cell division. RNA synthesis was unaffected by PMA treatment in SV40-3T3 and a 3,4-benzpyrene-transformed hamster embryo cell line. Nuclear RNA synthesis induced by PMA in 3T3 cells was partially resistant to the inhibitory effects of actinomycin D (1.0 µg/ml).

70-1472 THE EFFECT OF ANTILYMPHOCYTE SERUM ON THE INDUCTION AND GROWTH OF TUMOR IN THE ADULT MOUSE. (E.) Cerilli, G. J. (Ohio State U. Coll. Med., Columbus) and R. C. Treat. Transplantation 8(6):774-782, 1969.

The influence of rabbit anti-mouse lymphocyte serum (ALS; 0.25 ml every 3 days) on the growth of s.c. transplanted mouse mammary adenocarcinoma (H2712) in C3H/HeJ mice, and its ability to influence the incidence of sarcomas induced by 3-methylcholanthrene (MC; 1 mg s.c. in olive oil) in CBA mice was studied. ALS treatment of mice inj. with tumor cells significantly accelerated tumor growth when the tumor was transferred across the H-1 and H-2 histocompatibility barriers and eliminated pre-existing sensitization. ALS increased the incidence and shortened the latent period of MC-induced tumors. Absorption of ALS with viable tumor cells did not reduce its ability to accelerate tumor growth, although absorption with lymphocytes did. When incubated *in vitro* with ALS, tumor cells retained the ability to kill the host when admin. to normal mice. It is suggested that the influence of ALS is secondary to its immunosuppressive properties, and its ability to influence tumor growth is related to the absence of an inhibitor of tumor cell viability.

70-1473 THE ROLE OF ASCORBIC ACID IN THE PREVENTION OF BLADDER TUMOR FORMATION.

(E.) Schlegel, J. U. (Tulane U. Sch. Med., New Orleans, La.), G. E. Pipkin, R. Nishimura and G. N. Schultz. Trans. Amer. Ass. Genitourin. Surg. 61:85-89, 1969.

Pellets of cholesterol, 3-hydroxyanthranilic acid (OHA) or 3-hydroxy-5-carboxybenzoquinone-(2-hydroxy-6-carboxy-anil)-(1)imide-(4) [HCB] were implanted into bladders of 60-120-day-old female Swiss albino mice. Some animals also received L-ascorbate (250 mg%) in their drinking water *ad libitum*. The animals were sacrificed 40 weeks later. Mice implanted with OHA had significantly greater bladder tumor formation than any of the remaining groups, but admin. of ascorbic acid prevented OHA from exerting any specific carcinogenic effect. It is concluded that OHA alone is not carcinogenic and that the presence of an anti-oxidant in urine, in amounts sufficient to prevent oxidation of OHA, will also prevent increased bladder tumor formation. Animals implanted with HCB had no more bladder tumors than those implanted with cholesterol pellets, and it is concluded that HCB, which is an oxidative product of OHA, is non-carcinogenic for the mouse bladder.

70-1474 CHARACTERISTIC APPEARANCE OF ³H-LABELED-3-HYDROXYANTHRANILIC ACID IN THE URINARY BLADDER OF RATS WITH OR WITHOUT BLADDER TUMORS. (E.) Röhrl, L. (U. Heidelberg Clin. Surg., Germany), K. Hochberg and W. Kochen. Scand. J. Urol. Nephrol. 3(3):214-218, 1969.

After i.p. inj. of radioactive 3-hydroxyanthranilic acid (HAA; a tryptophan metabolite) into healthy rats and rats with HAA-induced urinary bladder tumors, autoradiography showed that radioactivity in the epithelium cells was located primarily in the upper cell layers of the bladder; but this activity was rarely located within the nucleus itself. Deposition within the epithelium of the urinary bladder of healthy rats was not as extensive as it was in tumor-bearing bladders. Deposition of radioactivity in the epithelium was much more pronounced than that found within the submucosa and muscularis. It is suggested that some tryptophan metabolites influence the production of bladder neoplasms.

70-1475 EXPERIMENTAL STUDIES OF BLOOD-BORNE METASTASIS AND INDUCED TUMOR IN INJURED LUNG. (E.) Matsushima, T. (Kumamoto U. Med. Sch., Japan). Kumamoto Med. J. 22(2): 83-98, 1969.

Female albino dd mice, with lungs injured by rabbit anti-mouse lung serum (0.1 or 0.2 ml), were admin. 4-nitroquinoline N-oxide (0.25 mg/week x 10, + cholesterol in olive oil, s.c.) and sacrificed in 222 days. Lung tumors were induced at the same rate in both serum-treated mice and controls, but mice with injured lungs developed larger, more numerous nodules. Nearly

all mice developed adenomas, and 2/12 and 1/15 treated and control mice, resp., developed adenocarcinomas.

70-1476 EFFECT OF ALKYL-BENZENESULFONATE AS A VEHICLE FOR 4-NITROQUINOLINE 1-OXIDE ON GASTRIC CARCINOGENESIS IN RATS. (E.) Takahashi, M. (Nagoya City U. Med. Sch., Japan). Gann 61(1):27-33, 1970.

Rats received 4-nitroquinoline 1-oxide (NQO; 1 mg in 1 ml 20% ethanol containing 8% alkyl-benzenesulfonate [ABS], 2-3 admin./week x 18, p.o.), NQO (1 mg in 1 ml 20% ethanol, 3 admin./week x 18) or 20% ethanol with 8% ABS (3 admin./week x 18). The 15 rats receiving NQO + ABS developed 2 adenocarcinomas, 1 hemangiosarcoma (1), and 1 hemangioma of the glandular stomach. Multiple papillomatous lesions, 5 squamous cell carcinomas, 2 giant squamous cell papillomas, and 1 hemangiosarcoma with squamous cell carcinoma were found in the forestomach of rats in this group. In rats receiving NQO without ABS, 1 liver sarcoma and benign papillomas of the forestomach developed in 9 rats. Stomach neoplasms were found in 0/10 rats who received ethanol + ABS. It is concluded that the surfactant ABS brings NQO in direct contact with the glandular epithelium, thereby promoting carcinogenesis.

70-1477 RELATION BETWEEN CARCINOGENICITY AND METABOLIC REDUCTION OF 4-NITROQUINOLINE 1-OXIDE DERIVATIVES. (E.) Araki, M. (Nat. Cancer Ctr. Res. Inst., Chuo-ku, Tokyo), T. Matsushima and T. Sugimura. Experientia 26(5): 528-529, 1970.

Derivatives of 4-nitroquinoline-1-oxide (4NQO) with substitutions at positions 2, 6 or 8, which could be enzymatically reduced to corresponding derivatives of 4-hydroxyaminoquinoline-1-oxide, were carcinogenic. Two analogs of 4NQO, 3-nitroquinoline-1-oxide and 5-nitroquinoline-1-oxide, were not carcinogenic.

70-1478 CARCINOGENIC ACTION OF HEXAMETHYL-DEWAR-BENZENE AND HEXAMETHYLBENZENE IN MICE. (Ger.) Dannenberg, H. (Max Planck Inst. Biochem., Munich, Germany), I. Brachmann and C. Thomas. Z. Krebsforsch. 74(1):100-102, 1970.

Hexamethyl-Dewar-benzene (hexamethylbicyclo (2.2.0)hexa-2,5-diene) and hexamethylbenzene were admin. to groups of 15 (8 male, 7 female) 3-mo.-old SaB mice, either s.c. (5 mg in 0.1 ml tricaprylin/4 weeks x 15) or by skin painting (0.4% soln. in acetone, 2 applications/week); the animals were observed for 18 mo. Among the males inj. with hexamethyl-Dewar-benzene, 1/8 developed leukemia (with infiltration of the liver and spleen) after 386 days and 1/8 developed a liver carcinoma after 378 days. A

small papilloma developed after 322 days in 1/2 females painted with hexamethylbenzene.

70-1479 LEUKEMIA IN MICE FED BENZO(A)PYRENE: A CLINICAL, PATHOLOGIC AND HEMATOLOGIC STUDY. (E.) Rigdon, R. H. (U. Texas Med. Branch, Galveston), M. C. Bengé, H. Kirchoff, J. Mack and J. Neal. Texas Rep. Biol. Med. 27(3): 803-820, 1969.

Admin. of 3,4-benzpyrene (BP; 0.25 mg/g of food) to CFW, AKR, BALB/c and A/Jax mice, induced leukemias and thymomas in CFW and AKR mice, and in 1 mouse of the A/Jax strain; neither tumor developed in BALB/c mice. Mice less than 40 days old developed leukemia more frequently than older mice (313 days) fed the same ration. Some CFW littermates developed leukemia, while others did not. The latent period, hematological characteristics of blood and bone marrow, and pathological changes in BP-fed mice were as variable as those of mice with Friend or Rauscher virus-induced leukemia.

70-1480 3,4-BENZPYRENE CONTENTS OF SOOT AND EXHAUST GASES FROM AIRCRAFT ENGINES OF THE TURBINE AND PISTON TYPE. (Rus.) Shabad, L. M. (Inst. Exp. Clin. Oncol., Moscow) and G. A. Smirnov. Gig. Sanit. 34(2):98-99, 1969.

Soot and exhaust gases emitted by aircraft engines were extracted by a Soxhlet apparatus or by shaking (shaking was a less efficient method than the use of the Soxhlet apparatus) and analyzed for 3,4-benzpyrene (BP) content by spectrography and potentiometry. Soot emitted by a turbine engine (from the TU-104 airplane) had a higher BP content than soots emitted by piston-type engines (from the IL-14 and AN-2 airplanes). Exhaust gases from "turboreactive" engines contained larger amounts of BP than exhaust gases from "turbospiral" engines, but the BP emission of a "turbospiral" engine during 1 min. of work (8000 revolutions/min.) was greater than the emission of a "turboreactive" engine during 1 min. of work (10,500 revolutions/min.; 4 and 2-4 mg of BP, resp.).

70-1481 CHANGES IN THE 3,4-BENZPYRENE CONTENT OF AUTOMOBILE EXHAUST GASES, IN RELATION TO THE NATURE OF THE ENGINE'S PERFORMANCE AND THE TYPE OF GASOLINE. (Rus.) Minaev, A. A. (Erisman Sci. Res. Inst. Hyg., Moscow). Gig. Sanit. 34(3):92-93, 1969.

In exhaust gases from an idling automobile engine with a properly-adjusted carburetor, the 3,4-benzpyrene (BP) content was highest at the lowest rpm (revolutions/min.) value. Without adjustment of the carburetor, fuel consumption increased by 30-60% and the BP content of the exhaust gas increased 2-4-fold. The BP content of the exhaust gases also depended upon the

quality of the gasoline used; with 1 type of fuel (designated A-72), the BP content of the exhaust was 10-15 times lower than with another gasoline (designated A-66). The av. BP output in exhaust gases from idling engines fueled with A-72 and A-66 was 5.270 and 47.730 $\mu\text{g}/\text{min.}$ of work, resp.; when the engines were run at 25-75% of capacity, av. BP output values with A-72 and A-66 were 0.006-2.416 and 2.127-15.450 $\mu\text{g}/\text{minute}$, resp. BP output in both cases was highest when the engine was run at 50% of capacity and lowest when the engine was run at 25% of capacity. Av. BP content in the air following 2 successive starts of 1 engine was 0.504 μg , compared to 0.832 μg in 3 successive starts of another engine (no other details).

70-1482 PLEUROPULMONARY ASBESTOSIS AND MALIGNANT PLEUROPULMONARY MESOTHELIOMA. (Fr.) Arnaud, A., G. Lebreuil, B. Raphael, H. Payan, M. Mongin and J. Charpin (St. Marguerite Hosp., Marseille, France). J. Franc. Med. Chir. Thorac. 23(1):85-94, 1969.

A pleural mesothelioma was confirmed by biopsy in a 64-yr.-old man with a history of probable, prolonged exposure to asbestos in the course of installing insulation in buildings and working as a carpenter in naval shipyards. The pt., who presented with a myocardial infarct, had experienced no symptoms of the tumor, which (as X-ray examination indicated) had spread from the base to the apex of the left pleura without giving rise to a pleural effusion. At autopsy, 3 mo. later, a few asbestos particles were found in the primary tumor, and numerous particles were located in the pulmonary parenchyma, the alveoli, the tubules of the terminal bronchioles and the bronchial mucosa. Metastases to the stomach, liver and adrenals were found.

70-1483 CIGARETTE SMOKE: THE EFFECT OF RESIDUE ON MITOCHONDRIAL STRUCTURE. (E.) Kennedy, J. R. (U. Tennessee, Knoxville) and A. M. Elliott. Science 168(3935):1097-1098, 1970.

Cells of *Tetrahymena pyriformis* were exposed to residue from mainstream cigarette smoke (residue from 1 cigarette/each 15 ml of cells). The mitochondria were particularly affected; degradation of internal membranes of mitochondria correlated with loss of ciliary activity and cell death. After exposure to residue for 7 min., the tubular arrangement of the inner mitochondrial membrane was altered, and shelflike mitochondrial cristae characteristic of higher cells appeared. After 42 min., most of the inner tubular membranes were destroyed. In cells exposed to residue for as long as 70 min., remnants of the inner tubular network persisted even when ciliary loss and cell death were imminent; these tubules were primarily along the periphery of the mitochondria. Most

mitochondria were similarly affected by the residue, but some were unaltered after as much as 70 min. It is suggested that only those mitochondria that are functionally active are altered by the cigarette smoke residue.

70-1484 LACK OF EFFECT OF SMOKING ON THE EXCRETION OF TRYPTOPHAN METABOLITES BY MAN. (E.) Brown, R. R. (U. Wisconsin Med. Sch., Madison), J. M. Price, S. W. Burney and G. H. Friedell. Cancer Res. 30(3):611-614, 1970.

The urinary excretion of 9 metabolites of tryptophan and niacin was determined after admin. of L-tryptophan (2.0 g, p.o.) in 12 normal smokers, in the same subjects after they stopped smoking for 3 weeks, and after they resumed smoking. Creatinine and 4-pyridoxic acid levels were also measured to test reliability of collections and index of nutrition. No significant changes occurred in the excretion of any of the metabolites, except for an inconsistent change in acetylkynurenine excretion. Additional studies which compared 17 male smokers (av. smoking history of 15 cigarettes/day for 9.5 yr.) with 13 male non-smokers revealed no differences in urinary excretion of these metabolites. It is suggested that the association between bladder cancer and smoking is not mediated by altered urinary excretion levels of niacin or tryptophan metabolites in smokers.

70-1485 ASYMPTOMATIC POLYPS OF THE RECTUM AND COLON. II. FREQUENCY, SMOKING, AND ARTERIOSCLEROTIC HEART DISEASE. (E.) Drexler, J. (130 N. La Cienega, Los Angeles, Calif.). Arch. Intern. Med. (Chicago) 121(1):62-66, 1968.

Proctoscopic examination was performed on 390 pts., 150 with coronary artery disease, and 240 without. Polyps of the colon and rectum were seen in 46% of the total group. No significant difference was seen between the 2 groups, or between men and women. However, especially in the studies done after July 1, 1965 (when more attention was paid to minute lesions), polyps seemed more frequent in pts. with coronary disease than in the pts. without coronary disease. A significant difference was seen between smokers (62%) and non-smokers (34%); the frequency of polyps in ex-smokers was 60%, compared to 48% in pipe and cigar smokers.

0-1486 RELATIONSHIP OF SELENIUM TO CANCER. I. INHIBITORY EFFECT OF SELENIUM ON CARCINOGENESIS. (E.) Shamberger, R. J. (Cleveland Clin. Found., Ohio). J. Nat. Cancer Inst. 44(4):931-936, 1970.

Sodium selenide (0.0005%) and vitamin E (0.13%) significantly reduced the number of 7,12-dimethylbenzanthracene (DMBA; 0.125 mg in 0.25

ml acetone)- and 3-methylcholanthrene (MC; 0.25 ml of 0.01% soln.)-induced skin tumors in mice in nondietary tumor promotion experiments. Both vitamin E and selenium (Se) reduced the total number of papillomas. Ascorbic acid (0.20%), hydrocortisone (0.15%) and chloroquine (0.05%) were ineffective. After admin. of sodium selenide, the number of mice with MC-induced papillomas and the number of cancers was not significantly reduced in 19 and 30 weeks, resp. Admin. of sodium selenite (1.0 ppm in a Torula yeast diet) significantly reduced the number of skin tumors induced by DMBA + croton oil and 3,4-benzpyrene. Tumor incidence was not decreased in mice fed a Torula diet with only 0.1 ppm sodium selenite or a commercial diet (Rockland). It is suggested that the inverse relationship between Se conc. and tumor formation is applicable to studies of cancer mortality in humans and Se levels, and the reduction of carcinogenesis.

70-1487 DEVELOPMENT OF HEPATOMAS IN RAINBOW TROUT IN RELATION TO THE DURATION OF ADMINISTRATION OF A DIET CONTAINING AFLATOXIN. (It.) Ghittino, P. (Inst. Exp. Zool., Turin, Italy), M. L. Codegone and A. Provana. Cancro 21(6):619-627, 1968.

Rainbow trout were fed a dry diet including 50% peanut meal containing aflatoxin B₁ (0.36 ppm) with traces of aflatoxin B₂; 1 mo. later, 7/20 showed foci of hepatic necrosis, 17/20 showed damaged liver cells and 10/20 showed cellular regeneration. Tabulations at the end of 2 mo. were comparable, except for a 50% increase of cellular regeneration; after 3 mo., results were 4/16, 14/16 and 14/16, resp., with 3/16 also showing microscopic hepatomas; and after 4 mo., they were 0/8, 6/8 and 6/8, resp., with 4/8 showing microscopic hepatomas. Of a group of fish fed the diet for only 1 mo., followed by a diet of fresh beef liver, 31.8% developed hepatomas after 9 mo., while 2-, 3- and 4-mo. feedings of the diet induced hepatomas in 100% of each group. A typical cholangioma was also found in 1/12 of the 2-mo.-feeding group. About 40% of these 9-mo. hepatomas were demonstrable macroscopically. Histologic studies suggest that liver cells damaged by aflatoxicosis undergo rapid necrosis, and are replaced by regenerative hepatocytes, some of which tend to become neoplastic.

70-1488 THE PATHOGENIC MOLD Aspergillus fumigatus AS A CAUSE OF MALIGNANT TUMORS. (Ger.) Teichmann, R. (Stephanstr. 1, Rostock, Germany). Z. Aertzl. Fortbild. 64(3): 143-146, 1970.

Culture fluid (0.3-0.5 ml) containing spores of Aspergillus fumigatus was inj. into mice; neoplastic ulcers of the intestine and liver developed in 2/15 animals. A significant increase in virulence was obtained by incubation

of the organism in tissue, blood or human serum cultures. Inj. of the *Aspergillus* toxin (afutoxin; an analog of aflatoxin; s.c.) induced a squamous cell carcinoma in the thoracic wall of 1/15 animals. It is suggested that certain environmental conditions cause the development of atypical polymorphous forms and other cell forms difficult to diagnose in tumor tissue.

70-1489 INFLUENCE OF GERM-FREE STATUS ON THE EXCRETION OF SIMPLE PHENOLS OF POSSIBLE SIGNIFICANCE IN TUMOUR PROMOTION. (E.) Bakke, O. M. (U. Bergen, Norway) and T. Midtvedt. *Experientia* 26(5):519, 1970.

The urinary excretion of simple phenols (some of which are carcinogenic; phenol, p-cresol and 2-ethylphenol potentiate tumor development in the skin of mice after application of dimethylbenzanthracene) was studied in germ-free and conventional CDF rats maintained on a commercial pellet diet. Except for traces of phenol (less than 0.005 mg/day), simple phenols were not found in the hydrolyzed urine of germ-free rats. Excretion of major urinary phenols occurred in conventional rats. The almost complete absence of urinary simple phenols is a previously unreported biochemical feature of germ-free animals; and it is suggested that, except for phenol which develops to a very small extent in tissues, normal microflora are essential for the formation of these compounds.

70-1490 EFFECT OF β -PROPIOLACTONE ON BACTERIOPHAGES AND *Salmonella typhimurium*. (E.) Fukuda, S. (Temple U. Sch. Med. Fels Res. Inst., Philadelphia, Pa.) and N. Yamamoto. *Cancer Res.* 30(3):830-833, 1970.

Salmonella typhimurium strains and bacteriophage P22 were inactivated by low conc. of β -propiolactone (BPL; 0.05%). Recombination-deficient (rec^-) mutants were inactivated drastically, UV light-sensitive (hcr^-) mutants were inactivated very rapidly and wild type mutants were inactivated slowly. BPL induced the prophage P221 from wild type and hcr^- mutants, but not from rec^- mutants. When BPL-damaged bacteriophage P22 was assayed simultaneously on hcr^- mutants, rec^- mutants and wild type, the survival of P22 on wild type was slightly higher than that on rec^- and hcr^- mutants. When a clear plaque-forming mutant (c_2) of P22 phage was treated with BPL and assayed on hosts either lysogenic or non-lysogenic for P221b, C+ plaques were seen among the survivors on the P221b lysogen, but no C+ plaques were found on the nonlysogens. It is concluded that BPL acts directly on phage DNA and results in inactivation, repair and recombination.

70-1491 EFFECT OF CARCINOGENS ON TISSUE PROLIFERATION (LIVER REGENERATION IN

MICE TREATED WITH CARBON TETRACHLORIDE). (Rus.) Chernina, L. A. (N. N. Petrov Res. Inst. Oncol., Leningrad, USSR). *Vop. Onkol.* 15(8):91-93, 1969.

In male albino mice, treatment with carbon tetrachloride (CCl_4 ; 0.04 ml x 1 s.c.), 2-45 days before partial hepatectomy, decreased mitotic activity in the regenerating liver. Survival rates after hepatectomy were 67% (12/18 mice) in untreated mice and 39% (48/123 mice) in CCl_4 -treated mice. The hepatectomy-induced changes in mitotic activity persisted for at least 1.5 mo.; the intensity of these changes showed cyclic changes, which resembled the fluctuations seen in other indices of liver reactivity in CCl_4 -treated mice.

70-1492 TRANSPLANTABLE BALB/c MOUSE TUMORS INDUCED BY MINERAL OIL. (It.) Fantini, F. (Via Francesco Sforza 35, Milan, Italy), A. Cantaboni, G. Galetti and F. Invernizzi. *Morgagni* 21(3):3-21, 1969.

Among pure strain BALB/c mice inj. with a liquid vaseline composed of saturated hydrocarbons (0.5 ml/dose, repeated several times at unspecified intervals i.p.), 8/80 developed plasmacytomas, 4/80 developed fibrosarcomas and 1/80 (each) developed leukemia and a hemangio-endothelioma. All of the tumors were sarcomatous in structure and developed from cells which were originally part of the oil granulomas. It is suggested that the distortion of tissue organization by physical, as contrasted to chemical or immunologic, intervention is important in the sequence of malignant transformation.

70-1493 BRAIN NERVE CELL TUMORS IN MICE ON DIETS SUPPLEMENTED WITH VARIOUS LIPIDS. (E.) Szepeswol, J. (U. Puerto Rico Sch. Med., San Juan). *Path. Microbiol.* 34(1):1-9, 1969.

The diet of T.M. strain mice was supplemented with small amounts of various lipids; 95 mice developed tumors located on the upper surface of the frontal lobe, varying in diameter from 2-5 mm. Many mice had multiple tumors. The brain tumor consisted mainly of differentiated nerve cells containing neurofibrils and Nissl bodies. The type of lipid supplement and the number of tumors which developed were as follows: cholesterol, 20/80 (25%); corn oil, 1/11 (9.1%); corn oil + cholesterol, 7/22 (31.8%); mono-olein, 3/63 (4.7%); mono-olein + cholesterol, 7/64 (10.9%); monostearin, 3/53 (5.6%); monostearin + cholesterol, 10/72 (13.8%); lecithin, 18/73 (24.6%); and lecithin + cholesterol, 27/88 (30.6%).

70-1494 INVESTIGATION OF FATTY ACIDS AND DERIVATIVES FOR CARCINOGENIC ACTIVITY. (E.) Swern, D. (Temple U. Sch. Med. Fels Res.

Inst., Philadelphia, Pa.), R. Wieder, M. McDonough, D. R. Meranze and M. B. Shimkin. Cancer Res. 30(4):1037-1046, 1970.

In mice admin. repeated s.c. inj. of 29 fatty acids and esters, lactones, and epoxy and peroxy compounds, inj. site sarcomas were induced by 12-hydroxystearic acid, methyl 12-hydroxystearate, 4-ketostearic acid, stearohydroxamic acid, glycidyl laurate, glycidyl oleate and p-nitro-peroxybenzoic acid. Lower doses of stearic acid and γ -stearolactone also induced sarcomas. It is concluded that weak carcinogens for the s.c. tissue of mice occur among these classes of chemical compounds.

70-1495 HISTOCHEMICAL STUDY ON RAT LIVER GLYCOGEN DURING DAB CARCINOGENESIS. (E.) Forget, A. (Montreal Cancer Inst. Res. Labs., Canada) and R. Daoust. Int. J. Cancer 5(3):404-409, 1970.

Male albino Wistar rats were fed a low protein, low-riboflavin diet containing 4-dimethylaminoazobenzene (DAB; 0.06%), and the distribution of glycogen in the livers of these animals was studied by the periodic acid-Schiff (PAS) reaction. Normal rat liver showed a relatively uniform distribution of both RNA and glycogen. In the early stages of DAB feeding, RNA and glycogen loss occurred in cells of centrolobular areas undergoing degeneration, but intense glycogen staining was seen in hyperplastic nodules that developed from cells of periportal areas. In later stages of DAB feeding, there was formation of hyperbasophilic foci accompanied by glycogen loss; hepatomas, which arose from such foci, were PAS-negative. A radical change in glycogen metabolism was thus associated with neoplastic transformation. It is suggested that hyperbasophilic foci are sites of modification in the regulation of the cell cycle that initiate neoplastic growth, and also of changes responsible for the secondary features of tumors.

70-1496 OXIDATIVE DEMETHYLATION OF N-METHYL-HYDRAZINES BY RAT LIVER MICROSOMES. (E.) Wittkop, J. A. (Oregon State U., Corvallis, Oreg.), R. A. Prough and D. J. Reed. Arch. Biochem. 134(2):308-315, 1969.

The demethylase enzyme system in the liver microsomes of Sprague-Dawley rats acted on 20 μ moles of 1,1-dimethylhydrazine, monomethylhydrazine, 1,2-dimethylhydrazine, procabazine and its azo derivative, yielding 176, 188, 63, 40 and 110 μ moles formaldehyde/5 mg protein/40 min., resp. Removal of molecular oxygen or the reduced nicotinamide adenine dinucleotide phosphate (NADPH)-regenerating system inhibited this activity, but in the latter case it was partially restored by addition of NADPH. Formaldehyde formation was enhanced by inj. of phenobarbital (100 mg/kg x 3 days) or with 3-methylcholanthrene (30 mg/kg x

2 days) prior to sacrifice, but inhibition of cytochrome P-450 by carbon monoxide, steapsin or deoxycholate nullified this effect. No inhibition was seen with SKF 525-A.

70-1497 ENZYME HISTOCHEMICAL STUDIES ON THE INTESTINES OF RATS DURING 1,2-DIMETHYL-HYDRAZINE CARCINOGENESIS. (Ger.) Völlnagel, T., F. Wildanger and A. Schauer (U. Munich Path. Inst., Germany). Z. Ges. Exp. Med. 151(3):208-213, 1969.

Sprague-Dawley and Wistar rats were admin. 1,2-dimethylhydrazine (DMH; 10, 30, 40 or 50 mg/kg/week) continuously (no other details). Loss or reduction of alkaline phosphatase, non-specific esterase and succinic dehydrogenase activity in the intestinal mucous membrane (attributed to general toxic cell damage) occurred only with the higher dosages (30-50 mg). Duodenal tumors induced by the low DMH dosage showed a loss of alkaline phosphatase activity, varied non-specific esterase activity and relatively high succinic dehydrogenase activity.

70-1498 EXISTENCE OF A HORMONAL FACTOR IN PULMONARY CARCINOGENESIS IN RESPONSE TO HYDRAZINE. (It.) Biancifiori, C. (Perugia State U., Italy). Lavori Ist. Anat. Univ. Perugia 29(1):29-41, 1969.

In intact and orchietomized (orx.) male CBA/Cb/Se mice receiving hydrazine sulfate (1 admin./day x 150, forced p.o.), the incidence of pulmonary tumors was tabulated by dose level as follows: 1.13 mg/day = 76% and 72%, resp.; 0.56 mg/day = 20% and 21%, resp.; 0.28 mg/day = 16% and 11%, resp.; 0.14 mg/day = 7% and 12%, resp., indicating no statistically significant differences between intact and orx. males. However, in intact and oophorectomized (oox.) virgin females, comparable tabulations were: 1.13 mg/day = 90% and 80%, resp.; 0.56 mg/day = 87% and 28%, resp.; 0.28 mg/day = 56% and 24%, resp.; 0.14 mg/day = 40% and 8%, resp., indicating highly significant differences between intact females and males and between intact and oox. females (except at the highest dose level). The action of a hormonal factor is suggested.

70-1499 FAILURE OF ARGININE GLUTAMATE TO INHIBIT LUNG TUMOR FORMATION BY ISONIAZID AND HYDRAZINE IN MICE. (E.) Yamamoto, R. S. (NCI, Bethesda, Md.) and J. H. Weisburger. Life Sci. 9, Pt. 2(5):285-289, 1970.

Admin. of L-arginine-L-glutamate (1% in the diet x 33, 39, 44 or 48 weeks) to 6-week-old, male A/J mice did not inhibit lung tumor induction by isoniazid (1 g/liter) or hydrazine sulfate (325 mg/liter) admin. in the drinking water. Number and multiplicity of lung tumors in controls was also unchanged. It is concluded

that arginine and its derivatives can detoxify hydrazine and related compounds in the liver, but not in the lung; a mechanism of competition at select membrane sites of target tissue is suggested.

70-1500 HEPATOMAS IN CBA/Cb/Se MICE AND LIVER LESIONS IN GOLDEN HAMSTERS INDUCED BY HYDRAZINE SULFATE. (E.) Biancificori, C. (Perugia U. Med. Sch. Inst. Path. Anat., Italy). *J. Nat. Cancer Inst.* 44(4):943-953, 1970.

Intact CBA/Cb/Se mice (male and female, 8 weeks old) were admin. hydrazine sulfate (HS; 0.14-1.3 mg/day in soln. x 150, p.o.). The incidence of hepatomas in males and females was 60% and 62.5%, resp. for the 1.13 mg dose, 48% and 66.6%, resp. (0.56 mg), 28% and 8%, resp. (0.28 mg) and 38% and 0%, resp. (0.14 mg). While most lesions were highly vascularized hepatocarcinomas, lung metastases were also found in 4 mice that received HS at 1.13 mg/day. In intact golden hamsters of both sexes, HS admin. caused liver reticuloendothelial cell proliferation and cirrhosis, degeneration of fibrous cells in hyalinized sclerotic tissue, and proliferation of bile ducts. No liver lesions developed in untreated controls.

70-1501 AN IMMUNOHISTOCHEMICAL STUDY OF ESTROGEN INDUCED PITUITARY ADENOMA IN RATS. (E.) Ueda, G. (Wakayama Med. Coll., Japan), J. Otsuka, T. Mori and K. Nagai. *Wakayama Med. Rep.* 13(2):49-58, 1968.

Female Wistar rats were Inj. with estradiol dipropionate (500 µg, every 10 days x 30 days or 5 mo.), and changes in pituitary glands studied by the fluorescent antibody technic. Normal pituitary glands contained 2 types of acidophils that secreted either prolactin or growth hormone. In rats admin. estrogen, hypertrophied chromophobic acidophils contained prolactin. Rats treated for 5 mo. developed microadenomas with hyperplastic cells (acidophilic or chromophobic) which contained prolactin. The unchanged growth hormone-secreting acidophils were usually found in adjacent tissue compressed by the microadenomas, and a few were admixed with the adenomatous growths. It is suggested that estrogen stimulates the pituitary tumor production by the prolactin-secreting acidophils, and that this may be a mixed tumor of 2 types of acidophils.

70-1502 ROLE OF THYROID HORMONES IN CARCINOGENESIS. (Rus.) Mandrik, E. V. (P. A. Gertsen Res. Inst. Oncol., Moscow) and A. P. Kashulina. *Vop. Onkol.* 15(8):65-67, 1969.

The effects of treatment with L-3,5,3'-triiodo-thyronine (T3; 0.05 µg/100 g/day x 2 weeks, then at 2-week intervals) on the induction of sarcomas by 3-methylcholanthrene (MC; 0.5 or 2.0 mg/100 g x 1 s.c.) were studied in male Wistar rats. The lower dose of MC, admin.

alone, induced sarcomas in 53.7% of 82 rats after 7 mo. At the higher dose, MC alone induced sarcomas in nearly all rats; only 1/66 (1.5%) was free of a sarcoma after 9 mo. of observation. When T3 was admin. during the latent period, following inj. of the larger dose of MC, 9/73 rats (12.3%) were tumor-free after 9 mo. Studies of several parameters of thyroid function (relative thyroid wt., ¹³¹I uptake by the thyroid and the height of the thyroid epithelial cells) showed that rats which developed no tumors, despite the inj. of effective doses of MC, had greater thyroid activity than either untreated controls or tumor-bearing rats. Admin. of T3 during the latent period enhanced thyroid function as well as increasing the number of animals resistant to tumor development.

70-1503 EFFECTS OF A CONTRACEPTIVE (OVULENE) ON MAMMARY CARCINOGENESIS IN THE MOUSE. (Fr.) Coezy, E. (Radium Inst. Genet. Lab., Paris) and G. Rudali. *Rev. Europ. Etud. Clin. Biol.* 15(2):205-209, 1970.

Virgin C3H mice were admin. Ovulene, a mixture of 90% ethynodiol and 10% mestranol (3 mg/kg feed, about 7.5 µg/day), beginning 2 weeks after the first estrus and continuing until natural death. Mammary tumors developed in 59% of treated mice; the mean latent period was 402 days and the mean survival time was 455 days. Comparable figures for controls were 71%, 426 days and 504 days, resp. For multiparous RIII mice, treated after ablation of a first tumor, results were 57%, 114-day mean latent period and 76%, 115-day latent period for controls. In hybrid (C3H x RIII) F₁ females, they were 97.5%, 233 days and 303 days, resp., compared to 92%, 277 days and 339 days, resp., for controls. For hybrid females treated p.o. with 30 µg/d Enovid, a mixture containing 1.5% mestranol (other components not indicated), they were 95%, 266 days and 327 days, resp. Ovulene had no effect on tumor incidence in C3H or RIII males bearing transplanted, spontaneous mammary adenocarcinomas, but survival times were reduced from 85 to 64 days and from 103 to 95 days, resp., as compared to controls. It is concluded that no significant modification of mammary carcinogenesis was seen with the products tested.

70-1504 INCREASED INCIDENCE OF MAMMARY TUMORS IN THE FEMALE RAT GRAFTED WITH MULTIPLE PITUITARIES. (E.) Welsch, C. W. (Michigan State U., East Lansing), T. W. Jenkins and J. Meites. *Cancer Res.* 30(4):1024-1029, 1970.

In female Sprague-Dawley rats, pituitaries were grafted unilaterally over the inguinal, abdominal and thoracic mammary glands and beneath the kidney capsule of each animal. Pituitaries were transplanted to mammary tumor-free 2-mo.-old nulliparous rats (Group I), 8-mo.-old

nulliparous rats (Group II) and 8-mo.-old multiparous rats (Group III), while mammary tumor-free nongrafted rats of comparable age and breeding status served as controls for each group. By 9 mo. after pituitary grafting, the number and percentage of rats with mammary tumors were: Group I, 13/45 (30%); Group II, 9/12 (75%) and Group III, 8/13 (61%), compared with 2/27 (7%), 1/12 (8%) and 3/16 (19%), resp., in the nongrafted controls. Pituitary homografts secrete relatively large amounts of prolactin and small amounts of all other pituitary hormones; therefore, these data indicate that an additional source of prolactin significantly enhances mammary tumorigenesis in the female rat.

70-1505 THE BINDING OF ESTRADIOL-17 β TO HUMAN BREAST CANCERS AND OTHER TISSUES *IN VITRO*. (E.) Johansson, H. (U. Uppsala, Sweden), L. Terenius and L. Thorén. Cancer Res. 30(3):692-698, 1970.

Material from malignant and benign human breast tumors was incubated with ^3H -labeled estradiol and the amount of receptor-bound estrogen was estimated. Significant binding of estradiol was found in 14/31 cancers, but in only 2/26 benign tumors. No obvious correlation was found between estradiol binding capacity of a cancer and factors of the disease at time of operation (differentiation of the tumor, histopathologic classification or clinical stage) or the menopausal stage. Binding of estradiol in normal tissue surrounding the tumor was not significant. It was possible to store material from experimental mammary tumors at 0° for 24 hours without change in estradiol binding capacity; at lower storage temperatures, it was destroyed.

70-1506 CONVERSION OF DEHYDROEPIANDROSTERONE, PREGNENOLONE, AND PROGESTERONE BY INTERSTITIAL CELL TUMOR TISSUE. (E.) Lucis, J. (Path. Inst., Halifax, Nova Scotia, Canada) and R. Lucis. Cancer Res. 30(3):702-708, 1970.

Biosynthesis of steroid was determined in a spontaneous mouse interstitial cell tumor grown as a s.c. transplant in isologous male recipients. Dehydroepiandrosterone was quickly converted to androstenedione by the tumor tissue; testosterone, 11β -hydroxytestosterone and 11β -hydroxyandrostenedione were formed at a slower rate. A conversion product with characteristics of 19α -hydroxyandrostenedione was also detected. After incubation with equal weights of ^3H -pregnenolone and ^{14}C -progesterone, dual labeling of progesterone, 7α -hydroxyprogesterone, testosterone, androstenedione, corticosterone, 20α -hydroxypregn-4-en-3-one and 11 -deoxycorticosterone was noted. A dual-labeled compound that resembled 11β -hydroxyprogesterone was also found. The biosynthetic properties of the tumor tissue resembled testis tissue in part and adrenocortical

tissue in part. The dual-labeled conversion products displayed variations in their ^3H : ^{14}C ratios attributable to heterogeneity of the tumor cell population and to differences in activities of steroid-transforming enzymes.

70-1507 STATISTICAL ANALYSIS OF HORMONAL EFFECTS ON THE STEROID RESPONSIVENESS OF SOLID EHRLICH TUMORS. (E.) Kodama, M. (Aichi Cancer Ctr. Res. Inst., Nagoya, Japan) and T. Kodama. Cancer Res. 30(1):221-227, 1970.

Hyperdiploid Ehrlich/2N carcinomas and hypotetraploid Ehrlich/4N carcinomas were implanted in SMA mice and tumor growth measured after 2 weeks, during which time various hormones were admin. Tumor growth, especially of the Ehrlich/4N tumor, was suppressed in males receiving hydrocortisone acetate (7 mg i.m.), but neither tumor was much affected in females. The mean tumor wt. in male mice admin. (1.4 or 7 mg) decreased with increased hormone dosage, with no significant difference between the 2 tumors. Mice orchiectomized or oophorectomized 1 mo. prior to tumor implantation and admin. testosterone (total 0.6 or 3 mg) starting 2 weeks before implantation, showed an increased tumor wt., parallel to the hormone dosage. In female mice, the Ehrlich/4N, but not the Ehrlich/2N tumors were stimulated by testosterone and testosterone derivatives (2-hydroxymethylene- 17α -methyl dihydrotestosterone).

70-1508 ACCELERATED INDUCTION OF HEPATOMA IN RATS FED N,N'-2,7-FLUORENYLENE-BISACETAMIDE BY X-IRRADIATION TO THE TARGET AREA. (E.) Nagayo, T. (Aichi Cancer Ctr. Res. Inst., Nagoya, Japan), M. Ito and S. Yamada. Gann 61(1):81-83, 1970.

Following X-irradiation (500 R/week x 20) to the stomach, Buffalo rats were fed N,N'-2,7-fluorenylenebisacetamide (FAA; 0.025% in the diet). Males admin. FAA developed hepatomas in the anterior half of the left lobes or on the left part of the middle lobes of the liver, but not in the right and caudate lobes; they also had stomach neoplasms. Female rats did not develop hepatoma nodules. Rats that received only X-irradiation had normal livers. It is concluded that X-irradiation combined with FAA has a synergistic carcinogenic effect on stomach mucosa, and on liver tissues as well.

70-1509 INFLUENCE OF AGE AND SEX ON HEPATIC LESIONS INDUCED BY CHEMICAL CARCINOGENS: INGESTION OF N-4-(4'-FLUOROBIPHENYL)ACETAMIDE BY BUFFALO STRAIN RATS. (E.) Stromberg, K. (NCI, Bethesda, Md.) and M. D. Reuber. J. Nat. Cancer Inst. 44(5):1047-1054, 1970.

A semisynthetic diet containing 0.04% N-4-(4'-fluorobiphenyl)acetamide was fed to 4-52-week-old inbred Buffalo rats of both sexes for 36

weeks. After 12 weeks, males developed more hepatic carcinomas than females, and young animals of both sexes had more hepatic lesions than older animals. In comparison to the other groups, the 4-week-old male rats had larger carcinomas, more carcinomas per liver, a higher incidence of pulmonary metastases, an increase in undifferentiated carcinomas and a shorter survival time.

70-1510 CARCINOGENICITY OF N-[4-(5-NITRO-2-FURYL)-2-THIAZOLYL]ACETAMIDE IN FEMALE RATS. (E.) Ertürk, E. (U. Wisconsin Med. Sch., Madison), S. M. Cohen and G. T. Bryan. Cancer Res. 30(4):936-941, 1970.

Female Sprague-Dawley rats were fed N-[4-(5-nitro-2-furyl)-2-thiazolyl]acetamide (0.199% by wt. x 46 weeks), followed by 20 weeks on a control diet. Of the animals that survived for 16 or more weeks, 52/56 had tumors localized as follows: salivary gland adenocarcinomas (6), alveolar cell carcinomas of the lung (7), transitional cell carcinomas of the kidney (2), mammary tumors (47; 24 fibroadenomas and 23 adenocarcinomas), skin tumors (3), intestinal adenocarcinoma (1) and splenic lymphosarcoma with hepatic metastases (1). Three mammary tumors (1 fibroadenoma, 1 adenofibroma and 1 adenocarcinoma) and 1 salivary gland adenocarcinoma were transplantable s.c. to weanling female Sprague-Dawley rats, inducing transplantable tumors in 7/24, 4/12, 9/12 and 14/24, resp. Of 9 mammary adenocarcinomas that grew in recipient rats, 2 became metastatic (1/2, through the abdominal wall and into the liver, 1/2 to the spleen).

70-1511 IMMUNOSUPPRESSIVE ACTIVITY OF METHYLCHOLANTHRENE IN THE MOUSE. A STUDY OF SECONDARY IMMUNE RESPONSE AND SURVIVAL. (Fr.) Salomon, J.-C. (Inst. Cancer Res., Villejuif, France), S. Gueguen and P. Lazar. Path. Biol. 18(1-2):65-68, 1970.

In 2-3-mo.-old C57/BL6 mice, immunized by i.p. inj. of the "H" antigen of *Salmonella typhosa*, treated i.m. 10 days later with 3-methylcholanthrene and admin. a second i.p. inj. of "H" antigen on day 19, mean antibody titers in the serum were identical to those in untreated controls. However, although a very high coefficient of correlation was found in the controls on days 8 and 9 after the first inj. of "H" antigen and on days 7 and 14 after the second, the coefficient of correlation among the treated animals was insignificant. This phenomenon is not attributed to the carcinogen, as the difference in antibody titer occurred before MC was admin. When the experiment was repeated, comparable coefficients of correlation were obtained for both controls and treated animals. Mean survival time among treated animals was 107 days, with no deaths among the controls. No demonstrable relationship was seen between the intensity of the immune

response, either before or after treatment with MC, and the duration of survival.

70-1512 HETEROLOGOUS ANTILYMPHOCYTE SERUM (ALS) HASTENS THE APPEARANCE OF METHYLCHOLANTHRENE-INDUCED TUMOURS IN MICE. (E.) Rabbat, A. G. (McGill U., Montreal, Canada) and H. F. Jeejeebhoy. Transplantation 9(2):164-166, 1970.

Male C57BL/6J mice were inj. with 3-methylcholanthrene (2 mg in 0.1 ml trioctanoin, s.c.). Two weeks later mice were admin. horse anti-mouse lymphocyte serum (ALS) or normal horse serum (0.25 ml 2 admin./week x 12). Tumors appeared earlier in the ALS-treated group. It is suggested that ALS depresses the inhibitory immune responses of tumor-specific antigens.

70-1513 HYDROXYUREA: SUPPRESSION OF TWO-STAGE CARCINOGENESIS IN MOUSE SKIN. (E.) Chan, P. C. (Amer. Health Found., New York, N. Y.), A. Goldman and E. L. Wynder. Science 168(3927):130-132, 1970.

Swiss mice received 7,12-dimethylbenzanthracene (50 µg in 50 µliters of acetone) applied to their backs. Four weeks later the mice were painted with 1% croton oil in acetone, and then received hydroxyurea (HU; 0.5 mg/g, i.p.) at 24 hours or at both 24 and 48 hours. Controls received an i.p. inj. of normal saline at 24 and 48 hours. Four days after the first application of croton oil, all mice were painted twice weekly with 1% croton oil for 14 weeks. HU admin. (24 and 48 hours after the first painting of croton oil) significantly reduced the tumor yield. Mice that received HU only at 24 hours after the first application of croton oil showed no significant difference in tumor yield.

70-1514 CHROMOSOMAL CHANGES IN 20-METHYLCHOLANTHRENE INDUCED SARCOMAS IN MICE IN RELATION TO TIME OF APPEARANCE OF THE TUMOURS. (E.) Hansteen, I.-L. (State Hosp. Inst. Gen. Exp. Path., Oslo) and S. B. Refsum. Virchow. Arch. [Zellpath.] 4(1):1-7, 1969.

Changes in chromosome numbers were found in 3-methylcholanthrene (MC; 1 mg in 0.1 ml benzene, s.c.)-induced sarcomas in mice. One or 2 stemlines (modes) were found in each tumor; stemlines were euploid in 2/6 tumors. Stemlines (modes) with near-diploid chromosome numbers were found in tumors appearing soon after admin. of MC, later tumors had stemlines with chromosome numbers between triploid and tetraploid. The rate of cell proliferation (RCP) was highest for early-appearing tumors and lower for later ones. A different RCP was sometimes found for different regions within the same tumor. No correlation was found between the great variation in the chromosome numbers and the degree of cell loss in tumors.

70-1515 CELL PROLIFERATION AND TIME OF APPEAR-
ANCE OF SARCOMAS INDUCED WITH 20-
METHYLCHOLANTHRENE IN MICE. (E.) Hansteen, I.-L.
(State Hosp. Inst. Gen. Exp. Path., Oslo) and
S. B. Refsum. Virchow. Arch. [Zellpath.] 4(1):
3-15, 1969.

Rate of cell proliferation (RCP) in sarcomas in-
duced in mice by 3-methylcholanthrene (1 mg in
0.1 ml benzene, s.c.) was correlated with time
required for tumor to reach about the same
diameter. With the possible exception of the
first 2/7 tumors, RCP decreased with increasing
time of development. Results of calculations
made on the number of possible volume doublings
in the tumors were consistent with the theory of
malignant transformation of a single cell. It
is suggested that because cell loss is an important
factor in the restricted size of some tumors com-
pared with RCP, a low RCP may explain the size
of some tumors.

70-1516 INEFFECTIVENESS OF POLY I:POLY C ON
TRANSPLANTED TUMORS INDUCED BY METHYL-
CHOLANTHRENE. (E.) Meier, H. (Jackson Lab.,
Bar Harbor, Maine), D. D. Myers and R. J. Huebner.
Naturwissenschaften 57(5):248-249, 1970.

Fibrosarcomas were induced in weanling mice of
the AKR/J, C57L/J and SWR/J strains by admin. of
methylcholanthrene (250 µg in 0.1 ml triolein;
s.c.). One tumor of each strain was then trans-
planted s.c. into weanling mice of the respective
ologous strain. These mice then received
either polyinosinic-polycytidylic acid (poly I:
poly C; 200 µg every 3 days to death; i.p.) or
phosphate buffered saline (PBS). The AKR/J
mice treated with poly-I:poly-C survived
significantly longer (56 days) than those given
PBS (39.4 days); tumor sizes at death were
identical. Tumor development was not prevented
and the size of transplanted fibrosarcomas was
not significantly altered by poly-I:poly-C in
any of the strains studied.

70-1517 EPITHELIAL CHANGES IN EMBRYONIC MOUSE
LUNG ORGAN CULTURES DURING TRANSPLACENTAL
ADMINISTRATION OF N-NITROSODIMETHYLAMINE AND N-
NITROSO-N-METHYLUREA. (Rus.) Smetanin, E. E.
(Inst. Exp. Clin. Oncol., Moscow). Vop. Onkol.
5(8):48-53, 1969.

Female C3HA or A mice received 2-3 s.c. inj. of
dimethylnitrosamine (DMNA; total 50 mg/kg) or N-
methyl-N-nitrosourea (MNU; total 75-100 mg/kg)
on days 20-21 of gestation. Lung tissue from 55
treated and 42 untreated embryos was explanted
and cultivated for up to 35 days. Explants from
embryos exposed to DMNA or MNU showed normal
morphology during the first 4 days of cultivation.
After 14 days or more of cultivation, diffuse
focal proliferation (resembling adenomatous
proliferation) was noted in 79% and 84% of the
available explants from DMNA- and MNU-exposed

embryos, resp. None of the explants from
untreated embryos showed this diffuse focal
proliferation. Disintegration of about 67% of
the cells of an explant was noted in 41% of the
control explants; in explants from DMNA- and MNU-
exposed embryos, this was seen in only 28% and
13% of the cultures, resp. Control explants
showed gradual degenerative changes after 3
weeks of cultivation and 12/28 had become
necrotic by day 28-35. The explants from DMNA-
or MNU-exposed embryos remained viable (with
persistent diffuse focal hyperplasia), and only
1/33 explants was necrotic by the end of the
observation period.

70-1518 THE EFFECT OF A SINGLE DOSE OF N-METHYL-
N-NITROSOUREA ON NUCLEIC ACID SYNTHESIS
IN VIVO. (Ger.) Kleihues, P. (Max Planck Inst.
Brain Res., Cologne-Merheim, Germany). Verh.
Deutsch. Ges. Path. 53:554-559, 1969.

Female Wistar rats (100-130 g) were admin. N-
methyl-N-nitrosourea (MNU; 50 or 100 mg/kg, single
i.p. dose) and either ³H-thymidine or ¹⁴C-orotic
acid (i.v., 30 min. before sacrifice), and the
synthesis of DNA and RNA was determined for
various organs (intestines, bone marrow, spleen,
kidney, liver) from 1.5-48 hours later. With
the 100 mg dose of thymidine, DNA synthesis was
inhibited 75%, 97% and 30% after 1.5, 6 and 48
hours, resp. With the 50 mg/kg dose, inhibition
was most pronounced after 3 hours (up to 90%),
but values quickly returned to normal levels.
Autoradiographic studies confirmed the strong
cytotoxic effect on proliferating cell populations
(crypt cells of intestines). Max. RNA inhibition
(27%, measured by labeling with ¹⁴C-orotate)
was seen for kidneys, intestines and spleen
(less than liver) after 1.5 hours, but values
quickly returned to normal and higher levels
within 24 hours. Studies of the effect of MNU
on different types of RNA indicated that the
compound has a greater inhibitory effect on
soluble than on nuclear or ribosomal RNA.

70-1519 ENZYME HISTOCHEMISTRY OF EXPERIMENTAL
BRAIN TUMORS IN RABBITS. (Ger.)
Stavrou, D. (U. Munich Inst. Oncol. Neuropath.,
Germany) and E. Dahme. Verh. Deutsch. Ges. Path.
53:548-553, 1969.

Admin. of N-methyl-N-nitrosourea (10 mg/kg
every 2 weeks, i.v.) to 40 chinchilla rabbits
resulted in brain tumors in 75% of animals after
an av. total dose of 660 mg/animal, (480-750 mg)
and an av. 268 day (210-349 days) induction period.
These tumors were classified as primary iso-
morphic gliomas (oligodendroglioma I and II,
glioblastoma), primary heteromorphic gliomas
(mixed gliomas) and ependymomas. The distribution
pattern and intensity of activity of different
hydrolases and oxidoreductases which differed in
different tumor types is described. In general,
a strong phosphatase, anaerobic transhydrogenase

and diaphorase activity was detected, while esterases, glycosidases, exopeptidases, aerobic transhydrogenases and oxidases showed weaker activity. The histochemical results show a good correlation with those obtained for human tumors of the central nervous system.

70-1520 AUTORADIOGRAPHIC LOCALIZATION OF TRITIATED 7,12-DIMETHYLBENZ(A)ANTHRACENE IN MAST CELLS OF HAIRLESS MOUSE SKIN. (E.) Tarnowski, W. M. (Ohio State U. Sch. Med., Columbus). Cancer Res. 30(4):1163-1167, 1970.

Biopsies were made at intervals from 30 min.-72 hours after application of a single dose of ^3H -7,12-dimethylbenzanthracene (200 μg) to the skin of female hairless mice. Labeling was seen in many, but not all, dermal mast cells in all of the specimens studied. The label was also found in the hair follicles, sebaceous glands and epidermis.

70-1521 SIMULTANEOUS RESPIRATORY AND HISTOLOGICAL STUDIES ON MOUSE SKIN DURING CARCINOGENESIS WITH DMBA. (E.) Zador, S. (Sydney U., Australia). Virchow. Arch. [Zellpath.] 4(1): 71-78, 1969.

In 50-day-old male white I.C. strain mice painted with 7,12-dimethylbenzanthracene (DMBA; 0.0025% in acetone; 2 applications/week for 1 mo., then 3 applications/week until sacrifice); respiration (O_2 uptake) and lactic acid formation were compared with the histologic appearance of skin at weekly intervals. DMBA produced no significant alterations in aerobic glycolysis before the appearance of tumors. The effect of DMBA on respiratory metabolism was cumulative; a sudden response occurred once the threshold was reached (in animals treated for more than 50 days). The O_2 uptake and lactic acid formation increased abruptly with appearance of tumors. This sudden change was not specific for DMBA-induced cancers, since it also was observed in papillomas. The metabolic changes were thus quantitative; they possibly occur in order to satisfy an increased energy demand set by the vastly increased number of cells found in the tumor, the mechanism occurring through physiological channels. These studies indicate that skin carcinomas, in contrast to all other tumors, have both an increased O_2 consumption and elevated lactic acid production.

70-1522 MECHANISM OF INDUCTION OF OVARIAN TUMORS IN THE MOUSE BY 7,12-DIMETHYLBENZ[a]ANTHRACENE. VII. RELATIVE ACTIVITIES OF PARENT HYDROCARBON AND SOME OF ITS METABOLITES. (E.) Jull, J. W. (U. British Columbia Cancer Res. Ctr., Vancouver, Canada) and A. Russell. J. Nat. Cancer Inst. 44(4):841-844, 1970.

When ovaries from CNZ mice admin. 7,12-dimethylbenzanthracene (DMBA; p.o.) were transplanted to

oophorectomized mice, the transplants developed granulosa cell tumors. No tumors developed in mice receiving 7,12-dihydroxymethylbenzanthracene or 7-hydroxymethyl-12-methylbenzanthracene. When ovaries in organ culture were exposed to DMBA or 12-hydroxymethyl-7-methylbenzanthracene for 4 days and reimplanted s.c., granulosa cell tumors developed in these implants. Similar results were seen in CNZ, C3H and CAF₁ mice. After treatment with 7-hydroxymethyl-12-methylbenzanthracene, 7,12-dihydroxymethylbenzanthracene or culture medium alone (as above), no ovarian tumors developed.

70-1523 THE EFFECT OF DIMETHYLBENZANTHRACENE ON THE INCORPORATION OF [^3H]THYMIDINE INTO DNA OF RAT MAMMARY GLAND AND UTERUS. (E.) King, R. J. B. (Imperial Cancer Res. Fund, London) and D. M. Cowan. Europ. J. Cancer 6(2):111-113, 1970.

The incorporation of ^3H -thymidine (^3H -TdR) into rat mammary gland DNA was higher in glands obtained at estrus than at proestrus, and decreased after oophorectomy (oov.). The effect of oov. was prevented by s.c. inj. of estradiol (10 $\mu\text{g}/\text{day} \times 3$). Incorporation of ^3H -TdR was greater in terminal buds of the mammary gland than in the central area of the gland. Benzanthracene (30 mg in 2 ml corn oil, p.o.) inhibited DNA synthesis in the mammary gland. Dimethylbenzanthracene (DMBA; as above) markedly inhibited ^3H -TdR incorporation into DNA of glands obtained at both estrus and proestrus, and also inhibited its incorporation into uterine DNA. It is concluded that inhibition of DNA synthesis by DMBA is not directly related to the carcinogenic action of this hydrocarbon.

70-1524 BINDING OF 7,12-DIMETHYLBENZ(a)ANTHRACENE AND BENZO(a)PYRENE TO NUCLEIC ACIDS AND PROTEINS OF ORGANS IN RATS. (E.) Prodi, G. (U. Bologna Inst. Gen. Path., Italy), P. Rocchi and S. Grilli. Cancer Res. 30(4): 1020-1023, 1970.

Wistar rats were inj. with ^3H -7,12-dimethylbenzanthracene (DMBA; 625 μC in 0.5 ml sterile olive oil i.p.) or 3,4-benzpyrene (BP; same dosage), and the activity of ribosomal RNA, DNA, nuclear and cytoplasmic proteins of skin, lung, liver, spleen and kidneys was studied. The amount of each agent bound to proteins was higher than that bound to nucleic acids and was different for the various organs, without a correlation between the level of activity of proteins and nucleic acids. DMBA was bound to a greater extent than BP. The DMBA/BP ratio was much higher for nucleic acids than for proteins, suggesting a preference of DMBA for nucleic acids as compared to BP.

70-1525 A COMPARATIVE STUDY OF THE ACTION OF CARCINOGENIC SUBSTANCES ON THE RNA

SYNTHESIS IN MOUSE SKIN. (E.) Alexandrov, K. (Sci. Res. Inst. Cancer Villejuif, France), C. Vendrely and R. Vendrely. Cancer Res. 30(4): 1192-1196, 1970.

Topical application of both 3,4-benzpyrene and 7,12-dimethylbenzanthracene to the skin of IC mice caused a preliminary decrease in the rate of RNA synthesis, followed by an abrupt increase well above the normal rate. The preliminary decrease occurred more rapidly with 3,4-benzpyrene. After application of the non-carcinogenic agent 1,2-benzpyrene, the only change noted was an increase in the rate of RNA synthesis. Electrophoretic study of skin RNA showed no differences between the RNA patterns for treated and normal skin.

70-1526 INFLUENCE OF IMMUNOSUPPRESSION AND IMMUNORESTORATION ON THE FORMATION OF URETHAN-INDUCED LUNG ADENOMAS. (E.) Trainin, N. (Weizmann Inst. Sci., Rehovot, Israel) and M. Linker-Israeli. J. Nat. Cancer Inst. 44(4): 893-900, 1970.

In inbred SWR/J and random-bred Swiss mice admin. urethan (U; 0.5 mg/g, i.p.), inj. with anti-lymphocytic serum (ALS; s.c.), significantly increased the incidence of U-induced lung adenomas, as compared with controls treated with normal rabbit serum (NRS). The mice also showed symptoms of immune impairment. When U-treated, neonatally thymectomized SWR/J mice were repeatedly implanted with syngeneic thymuses, immunological competence was restored and neoplastic response was reduced. Tumor incidence in these mice was similar to that of intact animals and significantly lower than that in thymectomized controls. It is concluded that impaired immunological competence is accompanied by an increase in the neoplastic response to U, which can be abolished when the immunological capacity of mice is restored.

70-1527 DEPRESSION OF WEAK ALLOGRAFT IMMUNITY IN THE MOUSE BY NEONATAL OR ADULT EXPOSURE TO URETHAN. (E.) Lappé, M. A. (Inst. Cancer Res., Philadelphia, Pa.) and D. S. Steinmuller. Cancer Res. 30(3):674-678, 1970.

In a series of experiments with 3 strains of mice, treatment with minimally carcinogenic doses of urethan impaired cellular immunity, as measured by prolongation of allograft survival. In adult mice, this effect was only detected at the highest dose of urethan used (150 mg/mouse), and was confined to the weaker strain combinations studied for allograft prolongation. Newborn mice were more susceptible to the depressive effect of urethan than were adults. For BALB/c strain mice, doses of 120 and 150 mg urethan did not prolong allograft survival in adults, but a dose of 1.0 mg admin. to 4-day-old males (but not females) significantly prolonged allograft survival at age 3 mo.

70-1528 METABOLITES INCLUDING A K-REGION. (Fr.) Raha, C. R. (U. Nebraska Coll. Med., Omaha). Bull. Soc. Chim. Biol. (Paris) 52(1):105-107, 1970.

By 72 hours after treatment of 20-week-old, female Swiss mice with 3,4-benzpyrene (4 mg x 1 i.p. in olive oil), the viscera yielded only metabolites with a K-region: a 4- or 5- ketonic derivative of 4,5-dihydrobenzpyrene (which could be transformed into benzpyrene 4,5-diacetate by Vollman's technique), chrysene, and 4 chrysene derivatives which underwent displacement in the presence of alkalis and were capable of being reduced to chrysene. None of the products previously reported in the literature were recovered. It is suggested that the ketone derivative may have originated in conjugates of a 4,5-dihydrodiol and chrysene in a compound which was bound to a protein, as previously reported for dibenz(a,h)anthracene.

70-1529 KINETICS OF DIMETHYLAMINE NITROSATION IN RELATION TO NITROSAMINE CARCINOGENESIS. (E.) Mirvish, S. S. (U. Nebraska Coll. Med. Eppley Inst. Res. Cancer, Omaha). J. Nat. Cancer Inst. 44(3):633-639, 1970.

Studies with ^3H -labeled dimethylamine (DMA) in buffered aqueous soln. showed that the rate of dimethylnitrosamine (DMN) formation at pH 3.4 was proportional to the DMA conc. and to the square of the nitrite conc.; the rate of reaction was max. at this pH. Although there were discrepancies at pH 1-2, the constancy of the appropriate rate constants under various conditions confirmed the third-order kinetics of the reaction. Rate constants can be used to determine the quantity of DMN formed in the stomach after ingestion of food containing various conc. of DMA and nitrite and during storage of this food.

70-1530 DISTRIBUTION OF BOUND TRITIUM FROM ^3H -DIETHYLNITROSAMINE IN RAT TISSUES. (E.) Rajewsky, M. F. (Max Planck Inst. Virus Res., Tubingen, Germany) and W. Dauber. Int. J. Cancer 5(3):389-393, 1970.

In adult male BDII rats admin. diethyl-(mono-2- ^3H)nitrosamine (DEN; 10 $\mu\text{g/g}$ p.o.), the conc. of bound ^3H was determined in liver, spleen, kidney, lung and small intestine as a function of time. At 240 hours after a single dose of ^3H -DEN, the highest relative conc. of bound ^3H was recorded in liver (1.00), followed by kidney (0.74), spleen (0.40), small intestine (0.18) and lung (0.14). The capacity of the liver for metabolic activation of DEN was not impaired at advanced stages of DEN hepatocarcinogenesis.

70-1531 EFFECT OF DIETHYLNITROSAMINE ON GLYCOGEN SYNTHESIS IN RAT LIVER. (Ger.) Sydow, G. (German Acad. Sci. Inst.

Cancer Res., Berlin-Buch) and F. Fey. Acta Biol. Med. German. 23(3):K9-K13, 1969.

Studies on glycogen storage and glucose-6-phosphatase activity in livers of male and female BD IX rats were performed 4-8 weeks after discontinuation of diethylnitrosamine (DENA; 1 mg/day x 75 and 120 days) admin. After 75 days the glycogen content in livers of female rats showed an 8-fold increase over control values (0.08% of fresh wt., compared to 0.01%, resp.), while the content in livers of males did not change. No sex-related differences were seen in controls. After 120 days the glycogen decreased in females to about 0.04%, but increased 50% in males (to 0.015%). In hepatomas the glycogen was increased 6-fold (0.054%). Histochemical studies showed that after DENA admin. the glycogen was stored in foci which were devoid of glucose-6-phosphatase activity, while the remaining areas had an enzyme activity similar to that in controls. No correlation between histological precancerous changes and glycogen storage was found. It is concluded that there is probably no causal relationship between areas of stored glycogen in precancerous rat liver and carcinogenesis.

70-1532 INACTIVATION OF TISSUE-SPECIFIC INHIBITORS BY A CARCINOGEN. (Ger.) Volm, M. (German Cancer Res. Ctr. Inst. Exp. Path., Heidelberg), V. Kinzel and R. Süß. Verh. Deutsch. Ges. Path. 53:560-565, 1969.

Extracts of livers from normal Sprague-Dawley and ACI rats contain a substance which significantly suppresses synthesis of DNA (as measured by ³H-thymidine incorporation) in liver explants in vitro. The substance was inactivated by pretreatment of the animals with diethylnitrosamine (DENA; 10 mg/kg i.v.), 4-6 hours, but not 16-24 hours, before excision of the livers, suggesting that the substance was reformed during that period. Extracts from regenerating livers (48 hours after partial hepatectomy) had the same activity as those from non-regenerating livers. DNA synthesis in kidney explants and cultures of L cells, embryonic hamster cells, Walker 256 carcinosarcoma and melanoma cells was also inhibited by liver extracts, but this inhibition was not abolished by pretreatment with DENA. Pretreatment with acetaminofluorene gave similar results. The presence of 2 different inhibiting substances in the liver is suggested: 1) a specific factor which acts only on liver cells and which can be inactivated by hepatocarcinogens, and 2) a non-specific factor which acts on other types of cells but is not inactivated by carcinogens. Extracts of hepatomas and ascites tumor cells showed no inhibitory effects and should not be used as reacting systems in studies of growth-regulating mechanisms.

70-1533 INDUCTION OF LIVER TUMOURS IN THE GUINEA PIG BY FEEDING DIMETHYLNITROSAMINE. (E.) Le Page, R. N. (U. Melbourne,

Australia) and G. S. Christie. Pathology 1(1):49-56, 1969.

Male guinea pigs received dimethylnitrosamine (DMN; 12.5-50 ppm/week x 7-49) in their diet, and changes in the liver and other organs were studied. Effects on animals given 12.5 or 25 ppm of DMN were mild, but those admin. 50 ppm initially gained wt. at a slower rate than controls and then lost wt. Malignant tumors of the liver cell type developed in 5 animals given 25 or 50 ppm DMN; induction time was 40-50 weeks for 50 ppm. Three of the tumors were rather undifferentiated and anaplastic, and 2 were more differentiated and had a more trabecular appearance. Metastatic spread of tumors occurred in the spleen and lungs. Because DMN appears to require activation in the liver before it can act as a carcinogen, it is suggested that the liver of the guinea pig possesses the microsomal enzyme system (N-demethylase) which causes enzymatic oxidative N-demethylation of DMN to produce a carcinogenic derivative.

70-1534 COMPARISON OF CELL PROLIFERATION KINETICS OF REGENERATING LIVER AND DIETHYLNITROSAMINE-INDUCED HEPATOCELLULAR CARCINOMAS AFTER HYPOPHYSECTOMY. (Ger.) Rabes, H. (U. Munich Path. Inst., Germany), R. Hartenstein and H. V. Tuzcek. Verh. Deutsch. Ges. Path. 53:565-569, 1969.

Hypophysectomy (hypox.) delayed DNA synthesis by prolonging the presynthetic G-1 phase of the generation cycle of regenerating (after partial hepatectomy) liver cells. This effect resulted from a prolongation of the interval between hepatectomy and the peaks of RNA and protein synthesis (from 13 to 27 hours and from 19 to 36 hours, resp.), which were essential for the start of DNA synthesis. A similar prolongation of the G-1 phase of the generation cycle after hypophysectomy was observed in diethylnitrosamine-induced hepatomas, but not in transplantable Zajdel ascites hepatomas of Wistar rats. After hypox., the induced autochthonous tumors showed the same prolongation of the generation cycle as for normal proliferating liver, while the more anaplastic transplantable ascites hepatoma cells became independent of the growth-regulating effect of the pituitary, and showed no change in the generation cycle.

70-1535 CARCINOGENIC ACTIVITY OF BUTYL-ETHYL-NITROSAMINE AFTER RECTAL APPLICATION IN RATS. (Ger.) Schmähl, D. (Inst. Exp. Toxicol. Chemother., Heidelberg, Germany). Z. Krebsforsch. 74(1):110-111, 1970.

Rectal admin. of butylethylnitrosamine (BEN; 50 mg/kg/week x 20) to 40 male 3-mo.-old Sprague-Dawley rats resulted in malignant liver tumors in 8 (3 carcinomas, 5 hemangioendotheliomas or sarcomas) and benign hepatomas in 7 animals.

Benign papillomas of the esophagus developed in 6 of the rats and hyperkeratoses of the mucous membrane of the esophagus developed in 3 animals. Toxic liver damage with hemorrhages and dystrophy of the organ caused death in 11 rats. It is concluded that BEN has a true organotropic (not a local carcinogenic) activity, and that the carcinogenic effect of non-symmetrical nitrosamines on the esophagus observed (previous experiments) after p.o. admin. is not due to a local effect of the compound.

70-1536 HISTOCHEMISTRY OF BUTYL-BUTANOL-NITRO-SAMINE INDUCED URINARY BLADDER CARCINOMAS. (Ger.) Kunze, E. (U. Munich Path. Inst., Germany), A. Schauer and M. A. Azami. Naturwissenschaften 57(6):310-311, 1970.

Admin. of N-butyl-N-4-butanolnitrosamine (20 mg/kg/day, in drinking water) to 10 female Wistar rats induced urinary bladder carcinomas after 120 days (no further details). These were classified as papillary, transitional epithelial, squamous cell or completely undifferentiated carcinomas. A nearly total loss of alkaline phosphatase was observed in the squamous cell and undifferentiated carcinomas, while the papillary and transition epithelial forms showed extensive areas devoid of this enzyme. NADH-diaphorase activity was either unchanged or slightly increased (except for squamous cell carcinoma which showed large areas devoid of this enzyme). Succinic dehydrogenase activity was unchanged or increased. In some carcinomas, groups of cells were detected which contained Periodic acid-Schiff positive granula in the Golgi zone. Studies of alkaline phosphatase and ³H-thymidine incorporation in the same histologic section revealed a higher labeling index in squamous cell and undifferentiated carcinoma than in those structures containing the enzyme.

70-1537 THE CARCINOGENIC EFFECT OF DIBUTYL-NITROSAMINE IN SYRIAN AND CHINESE HAMSTERS. (E.) Mohr, U. (Hannover Med. Tech. Sch., Germany), J. Althoff, D. Schmähl and F. W. Krüger. Z. Krebsforsch. 74(1):112-113, 1970.

Admin. of dibutylnitrosamine (DBN; 300 mg/kg/week x 30; p.o. or s.c.) to Syrian and Chinese hamsters induced tracheal papillomas, lung tumors, and some papillomas of the forestomach and urinary bladder in Syrian hamsters, while Chinese hamsters showed numerous papillomas of the forestomach and slight changes of the bladder epithelium. Bronchial adenomas and squamous cell carcinomas were also found in the Syrian hamsters. It is concluded that the 2 species of hamsters show different pathologic reactions to treatment with DBN.

70-1538 IN VIVO BINDING OF ACETYLAMINOFLUORENE (AAF) TO RAT LIVER TRANSFER RNA. (E.)

Agarwal, M. K. (Columbia U. Coll. Physicians Surg., New York, N. Y.) and I. B. Weinstein. Proc. Amer. Ass. Cancer Res. 10:2, 1969.

70-1539 TRANSPLANTABLE SUBCUTANEOUS SARCOMAS OF MICE INDUCED BY CARCINOSTATIC ANTIBIOTICS, MITOMYCIN C AND ACTINOMYCIN S AND THEIR RESISTANCES TO THE TREATMENTS. (E.) Akamatsu, Y. (Med. Coll. Georgia, Augusta) and R. Ikegami. Proc. Amer. Ass. Cancer Res. 10:2, 1969.

70-1540 BINDING OF N-HYDROXY-2-FLUORENYLACETAMIDE (N-OH-FAA) TO LIVER PROTEINS OF MALE RATS. (E.) Barry, E. J. (VA Hosp., Minneapolis, Minn.) and D. Malejka-Giganti. Proc. Amer. Ass. Cancer Res. 10:5, 1969.

70-1541 RELATIONSHIP BETWEEN LATENT PERIOD OF TUMOR INDUCTION AND ANTIGENIC STRENGTH. (E.) Bartlett, G. L. (Inst. Cancer Res., Philadelphia, Pa.) and R. T. Prehn. Proc. Amer. Ass. Cancer Res. 10:5, 1969.

70-1542 BEHAVIOR OF TUMOR PROMOTORS IN UNBURNED TOBACCO. (E.) Bock, F. G. (Roswell Park Mem. Inst., Buffalo, N. Y.). Proc. Amer. Ass. Cancer Res. 10:8, 1969.

70-1543 INFLUENCE OF POROSITY ON SARCOMA PRODUCTION BY SUBCUTANEOUS IMPLANTS. (E.) Brues, A. M. (Argonne Nat. Lab., Ill.), H. Auerbach, G. DeRoche and D. D. Grube. Proc. Amer. Ass. Cancer Res. 10:10, 1969.

70-1544 FOCUS OF SOLID-STATE CARCINOGENESIS. (E.) Bryson, G. (Cottage Hosp. Res. Inst., Santa Barbara, Calif.) and F. Bischoff. Proc. Amer. Ass. Cancer Res. 10:11, 1969.

70-1545 METABOLIC INHIBITION AND KILLING OF EHRlich MOUSE ASCITES CANCER CELLS BY TOBACCO SMOKE IN RELATION TO CARCINOGENESIS AND SMOKE FILTER EVALUATION AND IMPROVEMENT. (E.) Burk, D. (NCI, Bethesda, Md.), T. Howard and D. Tiggelbeck. Proc. Amer. Ass. Cancer Res. 10:11, 1969.

70-1546 AZULENO[5,6,7-cd]PHENALENE, THE FIRST NON-AROMATIC CARCINOGENIC HYDROCARBON. (E.) Buu-Hoi, N. P. (Nat. Ctr., Sci. Res., Paris), N. B. Giao and C. Jutz. Proc. Amer. Ass. Cancer Res. 10:12, 1969.

70-1547 TUMORIGENESIS IN RF MICE AS INFLUENCED BY CUMULATIVE DOSE OF DIETHYLNITRO-SAMINE (DEN). (E.) Clapp, N. K. (Oak Ridge

Nat. Lab., Tenn.) and A. W. Craig. Proc. Amer. Ass. Cancer Res. 10:14, 1969.

70-1548 CARCINOGENICITY OF 2-(2-FORMYLHYDRAZINO)-4-(5-NITRO-2-FURYL)THIAZOLE (FNT) AND STRUCTURALLY RELATED COMPOUNDS. (E.) Cohen, S. M. (U. Wisconsin Med. Sch., Madison), J. M. Price, F. J. Ansfield and G. T. Bryan. Proc. Amer. Ass. Cancer Res. 10:15, 1969.

70-1549 HISTOCHEMICAL STUDY ON LIVER GLYCOGEN DURING AZO-DYE CARCINOGENESIS. (E.) Daoust, R. (Montreal Inst. Cancer, Canada) and A. Forget. Proc. Amer. Ass. Cancer Res. 10:17, 1969.

70-1550 N-HYDROXY-2-ACETYLAMINOFLUORENE (N-HO-AAF) SULFOTRANSFERASE ACTIVITY IN VITRO, METHIONYL-BOUND AAF IN VIVO, AND CARCINOGENICITY OF N-HO-AAF IN RODENT LIVERS. (E.) DeBaun, J. R. (U. Wisconsin McArdle Lab., Madison), E. C. Miller and J. A. Miller. Proc. Amer. Ass. Cancer Res. 10:18, 1969.

70-1551 THE CONVERSION OF BENZOPYRENE TO WATER-SOLUBLE DERIVATIVES IN HAMSTER EMBRYO CELL CULTURES. (E.) Diamond, L. (Wistar Inst., Philadelphia, Pa.). Proc. Amer. Ass. Cancer Res. 10:19, 1969.

70-1552 CELL-FREE PASSAGE OF CHEMICALLY INDUCED THYMIC LYMPHOMA IN C57BL MICE. (E.) Doell, R. G. (Stanford U., Calif.). Proc. Amer. Ass. Cancer Res. 10:20, 1969.

70-1553 IN VITRO TRANSFORMATION OF HAMSTER EMBRYO CELLS BY CARCINOGENIC HYDROCARBONS. (E.) DiPaolo, J. A. (NCI, Bethesda, Md.), P. Donovan and R. Nelson. Proc. Amer. Ass. Cancer Res. 10:20, 1969.

70-1554 CANCER OF THE UTERINE CERVIX INDUCED IN BABL/C MICE BY AN ANTI-FERTILITY DRUG. (E.) Dunn, T. B. (NCI, Bethesda, Md.). Proc. Amer. Ass. Cancer Res. 10:21, 1969.

70-1555 A PRACTICAL TEST FOR CHEMICAL MUTAGENS IN MICE. (E.) Epstein, S. S. (Child. Cancer Res. Found., Boston, Mass.). Proc. Amer. Ass. Cancer Res. 10:22, 1969.

70-1556 PATHOGENESIS AND TRANSPLANTABILITY OF URINARY TRACT CARCINOMAS INDUCED BY N-[4-(5-NITRO-2-FURYL)-2-THIAZOLYL]FORMAMIDE (FANFT). (E.) Ertürk, E. (U. Wisconsin Sch. Med., Madison), J. M. Price and G. T. Bryan. Proc. Amer. Ass. Cancer Res. 10:23, 1969.

See also abstract nos.: 1439,1440,1441,1442,1459,1461,1567,1578,1598,1619,1621,1652,1653,1654,1655,1656,1657,1658,1659,1660,1661,1663,1698,1699

70-1557 CHANGES IN THE THYMOLYMPHOID AND MYELOID SYSTEMS OF THE MOUSE FOLLOWING A SINGLE INJECTION OF METHYLNITROSOUREA (MNUA). (E.) Frei, J. V. (U. Western Ontario Cancer Res. Lab., London, Canada). Proc. Amer. Ass. Cancer Res. 10:26, 1969.

70-1558 GROWTH CHARACTERISTICS AND MORPHOLOGY OF NEW LINES OF TRANSPLANTABLE RAT MAMMARY TUMORS. (E.) Friedell, G. H. (New England Deaconess Hosp. Cancer Res. Inst., Boston, Mass.) and W. F. Dunning. Proc. Amer. Ass. Cancer Res. 10:27, 1969.

70-1559 MATHEMATICAL CONSIDERATIONS IN THE CARCINOGENICITY OF MULTIPLE SUB-CARCINOGENIC DOSES. (E.) Furst, A. (U. San Francisco Inst. Chem. Biol., Calif.) and G. Ledin, Jr. Proc. Amer. Ass. Cancer Res. 10:28, 1969.

70-1560 LIVER CELL TURNOVER IN EARLY HEPATIC CARCINOGENESIS BY 2-ACETYLAMINOFLUORENE (AAF). (E.) Gardner, D. (New York U. Med. Ctr., N. Y.), R. Albert and W. Troll. Proc. Amer. Ass. Cancer Res. 10:28, 1969.

70-1561 EVALUATION OF NEOPLASTIC TRANSFORMATION IN VITRO. (E.) Goetz, I. E. (City of Hope Med. Ctr., Duarte, Calif.), B. R. Hill and R. Kinosita. Proc. Amer. Ass. Cancer Res. 10:30, 1969.

70-1562 STRUCTURE-ACTIVITY RELATIONSHIPS OF N-DISUBSTITUTED ARYLHYDROXYLAMINES. (E.) Gutmann, H. R. (U. Minnesota, Minneapolis), C. C. Chen and D. Leaf. Proc. Amer. Ass. Cancer Res. 10:34, 1969.

70-1563 PLURIPOTENT ONCOGENICITY OF 1,1-DIPHENYL-2-PROPYNYL-N-CYCLOHEXYL-CARBAMATE (I). (E.) Harris, P. N. (Eli Lilly & Co., Greenfield, Ind.), W. R. Gibson and R. D. Dillard. Proc. Amer. Ass. Cancer Res. 10:35, 1969.

70-1564 INCORPORATION OF THYMIDINE, URIDINE AND LEUCINE IN THE SKIN OF MICE AFTER TREATMENT WITH CROTON OIL FACTOR A₁ (TPA). Hecker, E. (German Cancer Res. Ctr. Inst. Biochem., Heidelberg) and H. Bresch. Proc. Amer. Ass. Cancer Res. 10:37, 1969.

70-1565 ENDOTOXIN'S INFLUENCE ON THE PRODUCTION OF SKIN PAPILLOMAS IN BALB/c MICE WITH METHYLCHOLANTHRENE. (E.) Henderson, J. S. (Rockefeller U., New York, N. Y.). Proc. Amer. Ass. Cancer Res. 10:37, 1969.

70-1566 VIRUS-INDUCED HEMOLYTIC ANEMIA IN MICE. (E.) Wollmann, R. L. (U. Chicago Pritzker Sch. Med., Ill.), E. J. Pang, A. E. Evans and W. H. Kirsten. Cancer Res. 30(4): 1003-1010, 1970.

Serial hematological profiles of mouse erythroblastosis virus (MEV)-infected C3Hf/gs mice and survival times of ⁵¹Cr-labeled RBC in normal and MEV-infected recipients showed that anemia was due to RBC destruction and that the accompanying splenomegaly was due to compensatory hyperplasia of RBC precursors. Splenectomy prevented secondary reticulocytosis, but did not prevent RBC destruction. Electron microscopy of peripheral blood from mice infected with MEV showed budding virus particles at platelet and reticulo- cyte cell surfaces.

70-1567 MORPHOLOGY OF VIRUS-LIKE PARTICLES PERSISTING IN MURINE EPENDYMOBLASTOMA IN VITRO. (E.) Ames, R. P. (Roosevelt Hosp., New York, N. Y.) and R. C. Rubin. Cancer Res. 30(4):1142-1148, 1970.

An ependyoblastoma originally induced by implantation of methylcholanthrene pellets into brains of C57BL/J mice was explanted into cell culture. The tumor cells grew in culture and virus-like particles persisted in the cells for up to 5 mo. The particles corresponded to intracytoplasmic A particles and extracellular enveloped A and B particles of the murine RNA tumor group; the particles were morphologically like the mammary tumor agent. Two unusual results of this study were the occurrence of B particles in non-mammary tissue and their long-term persistence in tissue culture.

70-1568 EFFECT OF VARIOUS FACTORS INVOLVED IN MAINTAINING ERYTHROPOIETIC HOMEOSTASIS ON THE COURSE OF FRIEND'S LEUKEMIA. (Fr.) Tambourin, P. (INSERM Radium Inst., Orsay, France), F. Wendling, N. Barat and F. Zajdela. Nouv. Rev. Franc. Hemat. 9(4):461-484, 1969.

In young male Swiss mice, blockage of endogenous erythropoiesis by transfusion polycythemia significantly inhibited the development of splenomegaly induced by Friend leukemia virus and partially reversed that which was already established, prolonging survival time by several mo. Actinomycin D, in doses which suppressed erythropoiesis entirely, also completely inhibited virus-induced splenomegaly, without interfering with other hematopoietic activity. Stimulation of erythropoiesis by repeated bleeding significantly increased the rate at which virus-induced splenomegaly developed. Inj. of phenylhydrazine hydrochloride had an even more pronounced effect, and also increased the rate at which the spleen was invaded by hyperbasophilic elements.

When inj. at 12 and 36 hours after inoc. of the virus, erythropoietin partially inhibited the effects of transfusion polycythemia on both erythropoiesis and virus-induced splenomegaly (the latter effect was not seen when it was inj. at 48 and 72 hours before or 5 and 7 days after inoc. of the virus). Electron microscopic studies demonstrated budding virus in cellular membranes at all stages of maturation.

70-1569 EVIDENCE OF AN INHIBITOR OF FRIEND LEUKAEMIA. (E.) Jasmin, C. (Paul-Brousse Hosp. Inst. Cancer Immunogenet., Villejuif, France), J. C. Chermann, G. Mathé and M. Raynaud. Rev. Europ. Etud. Clin. Biol. 15(1):56-60, 1970.

A strong inhibitor of Friend leukemia virus (FLV) was recovered, after precipitation with polyethylene glycol, from the supernatant of JLSV5 tissue cultures chronically infected with Rauscher leukemia virus. The inhibitor was not found in supernatants of an uninfected cell line or a rat cell line producing Moloney sarcoma virus *in vitro*. When inj. 4 days before or simultaneously with FLV, the inhibitor afforded almost complete protection against FLV for 3 weeks, but did not induce interferon production. It is concluded that production of this inhibitor may explain the large number of FLV virus particles required to induce leukemia in mice.

70-1570 EFFECT OF THE INJECTION OF A MURINE LEUKEMOGENIC VIRUS (FRIEND) ON THE IMMUNE REACTIONS OF SENSITIVE AND RESISTANT MICE. (Fr.) Schneider, M. (Paul-Brousse Hosp. Inst. Cancer Immunogenet, Villejuif, France) and J. F. Doré. Rev. Franc. Etud. Clin. Biol. 14(10):1010-1014, 1969.

Clearance of ¹³¹I-labeled human albumin was identical in normal immunized CBA mice and in CBA mice receiving Friend leukemia virus (FLV) 5 days before immunization. It was slightly, but not significantly, accelerated in C57BL/6 mice treated with FLV 5 or 21 days before immunization, as compared to C57BL/6 controls. None of the groups showed any significant difference with respect to the time required to reject C57Br skin grafts. Formation of hemolytic plaques against sheep RBC was greatly depressed in (DBA/2 x C57BL/6) F1 mice, 5 and 20 days after receiving FLV, and in C57BL/6 mice, 5 days after inj. of FLV. Production of a graft-versus-host reaction in (DBA/2 x CBA) F1 mice by lymph node cells of CBA mice treated with FLV 5 days previously was normal. In the case of C57BL/6 mice, 5 or 21 days after FLV inj., the reaction induced in (DBA/2 x C57BL/6) F1 mice was markedly increased. It is concluded that the immunosuppressive effects of FLV depend on genetic susceptibility of the mice.

70-1571 BIOCHEMICAL ASPECTS OF LEUKEMIA VIRUS-INDUCED IMMUNOSUPPRESSION: EFFECT OF FRIEND DISEASE VIRUS ON SPLEEN NUCLEASES AND NUCLEIC ACIDS. (E.) Chakrabarty, A. K. (Albert Einstein Med. Ctr., Philadelphia, Pa.), H. Friedman and W. S. Ceglowski. Cancer Res. 30(3):617-624, 1970.

The effect of Friend leukemia virus infection on spleen acid nuclease activity in female BALB/c mice was studied. Within 3-12 days after infection there was an 80-90% or more suppression of RNase activity, which remained depressed throughout a net period of 12 days; DNase decreased sharply during the first 3 days after infection and then returned to near normal levels. There was little change in total DNA content of spleen tissue in infected mice, whereas RNA levels decreased moderately and then increased sharply during the first week of infection. Little RNase activity was found in the nuclear, microsomal and mitochondrial fraction of spleens of infected mice, as compared to significant amounts of this enzyme in similar fractions of normal spleens. No significant difference was found in the localization, distribution and quantity of DNase activity in subcellular splenic fractions of normal or control mice. There was a slight decrease in DNase activity in the nuclear and supernatant fractions in infected spleens. Although most of the RNA in spleens of both infected and control animals was in the microsomal fractions, there was twice as much RNA (in this fraction) in the infected spleens. Little or no significant difference was found in the DNA content of the various subcellular fractions of normal or infected mice.

70-1572 INDUCTION OF LEUKEMIA IN BALB MICE BY ALLOGENEIC AKR LEUKEMIC CELLS. (E.) Pasqualini, C. D. (Inst. Hemat. Res., Buenos Aires), F. Saal, R. C. Braylan and S. L. Rabasa. Int. J. Cancer 5(3):338-345, 1970.

Short-latency leukemia developed within 24 days after intrasplenic inoc. of AKR lymphoma cells into 1-mo.-old BALB mice, followed by syngeneic i.p. passage; the av. incidence of leukemia was 83% in 88 mice. Intracisternal Type A and extracellular Type C viral particles were found in leukemic lymph nodes. These data were for 8 AKR lymphoma inocula out of 107 trials and were never seen in BALB controls and with normal AKR spleen inocula, except in 1 animal. The incidence of long-latency leukemia (av. 19 mo.) in surviving groups significantly increased to 45% in mice that had received AKR lymphoma inocula, as compared to 30% in those receiving normal AKR spleen inocula. There was a 15% spontaneous incidence in the BALB strain. Antigenic studies showed the presence of the Gross antigen in both short- and long-latency leukemias.

70-1573 STATOLON-THERAPY OF SPONTANEOUS VIRAL-CAUSED MOUSE TUMORS. (E.) Meier, H.

(Jackson Lab., Bar Harbor, Maine), D. D. Myers and R. J. Huebner. Naturwissenschaften 57(6): 310, 1970.

AKR/J and SJL/J mice, which develop leukemias and Hodgkin's disease-like reticulum cell sarcomas, resp., and have high leukemia virus titers, were treated with statolon (S; 25 mg/0.5 ml of 1% NaHCO₃/week x 5-7, i.p.). S induced peritoneal foreign-body granulomas in most mice. AKR/J mice admin. S for 6 wks. exhibited increased mortality from toxicity; their lifespan was significantly reduced and a highly significant wt. loss occurred in the liver, spleen and thymus. The inhibitory effect on lymphoreticular organs was associated with a significant decrease in tumor incidence. The wt. of lymphoid tissues was also reduced in SJL/J mice, although the tumor incidence was not significantly altered by S. It is concluded that therapy of spontaneous tumors is more difficult than that of induced and transplanted tumors, and that different therapeutic problems exist for the 2 types of tumors, leukemia and reticulum-cell sarcoma.

70-1574 IMMUNE REACTIONS IN LEUKEMIC OR PRE-LEUKEMIC AKR MICE. (Fr.) Doré, J. F. (Paul-Brousse Hosp. Inst. Cancer, Immunogenet., Villejuif, France), M. Schneider and G. Mathé. Rev. Franc. Etud. Clin. Biol. 14(10):1003-1007, 1969.

As compared to 3-mo.-old C57Br controls, the immune responses of 2-mo.-old, non-leukemic, AKR mice to relatively weak antigenic stimuli were significantly impaired. Clearance of ¹³¹I-labeled, human albumin was identical in the 2 groups, and in 8-mo.-old, leukemic AKR mice, as was the time required for rejection of C57BL/6 skin grafts (which bear different genes than C57Br and AkR cells at locus H-2). Rejection of C3H skin grafts (which bear the same genes as C57Br and AkR cells at locus H-2) was somewhat slower in the 8-mo.-old and significantly slower in the 2-mo.-old AKR mice, as compared to controls. Splenic production of hemolytic plaques against sheep RBC was normal in immunized 8-mo.-old mice, but significantly decreased in immunized 2-mo.-old AKR mice. Lymph node cells from 3-mo.-old, non-leukemic AKR mice failed to induce a graft-versus-host reaction in (AKR x C57Br) F₁ mice, although those from the C57Br controls induced a fatal reaction. It is suggested that an immunological deficiency syndrome is among the characteristics of the pre-leukemic state in AKR mice.

70-1575 INDUCTION OF AN ISOGENEIC GROSS VIRUS LEUKEMIA IN ADULT C57BL/6 MICE BY REPEATED INJECTIONS OF LEUKEMIC AKR CELLS. (Fr.) Amiel, J. L. (Paul-Brousse Hosp. Inst. Cancer Immunogenet., Villejuif, France) and M. Berardet. Rev. Franc. Etud. Clin. Biol. 14(6):587-589, 1969.

A suspension of splenic, thymic and lymph node cells from AKR mice bearing Gross virus leukemia was inoc. into 30-60-day-old, C57BL/6 mice. Leukemic ascites were demonstrable after 4 weeks. In other mice of the same strain, s.c. inj. of splenic cells gave rise to a palpable s.c. tumor by day 6, followed by death on about day 16. The original C57BL/6 cell line was also maintained by i.p. inj. of splenic cells and by peritoneal inoc. of ascitic cells. A collateral line was established in 2-mo.-old, (DBA₂ x C57BL/6) F₁ mice which received s.c. inj. of splenic cells from C57BL/6 donors; this line was maintained by s.c. inj. However, similar treatment of 2-mo.-old DBA₂ and AKR mice merely induced an s.c. tumor on day 6, which began to regress on day 8 and disappeared entirely by day 16. No acceleration of the appearance of spontaneous leukemia was noted in AKR mice.

70-1576 INDUCTION OF GROSS VIRUS LEUKEMIA IN ADULT C57BL/6 MICE BY INJECTION OF AKR CELLS (K36). (Fr.) Ajuria, E. (Paul-Brousse Hosp. Inst. Cancer Immunogenet., Villejuif, France), M. Doré and J. F. Doré. Rev. Franc. Etud. Clin. Biol. 14(7):700-703, 1969.

Cells from a K36 lymphoma (a spontaneous lymphoma in AKR mice, which was converted into ascites and maintained by homotransplantation in 2-mo.-old, non-leukemic females) were inoc. into C57BL/6 female mice. Very marked ascites developed in the hosts in 45-49 days. In recipient animals of the same strain, considerable ascites developed by day 6, followed by death on days 10-13. The cell line was maintained by i.p. inj. of ascitic fluid into animals of the same strain every 7 days. The cell line was incapable of inducing ascites or tumor in non-leukemic, 2-mo.-old, female AKR mice. Electron microscopic study of the cell line revealed lymphoblast-like cells with a cytoplasm rich in free ribosomes and containing virus particles similar to those found in spontaneous AKR leukemias. It is suggested that the specificity exhibited by Gross and other leukemia viruses is due more to immunological than to genetic factors.

70-1577 INFLUENCE OF TOYOCAMYCIN ON AVIAN LEUKEMIA MYELOBLASTS: CELL GROWTH, ULTRASTRUCTURE, RNA SYNTHESIS, AND ELABORATION OF BAI STRAIN A VIRUS. (E.) Bonar, R. A. (Duke U. Med. Ctr., Durham, N. C.), J. F. Chabot, A. J. Langlois, L. Sverak, L. Vepřek and J. W. Beard. Cancer Res. 30(3):753-762, 1970.

Myeloblasts from chickens with leukemia induced by avian myeloblastosis virus (AMV; BAI strain A) were cultured in vitro and treated with toyocamycin (TCM; 0.1-8.0 µg/ml). Cell growth was inhibited with an initial rate of decline of viable cell number proportional to TCM conc. Culture survival time was similar for all conc. 1 greater than 1 µg/ml. Virus elaboration by viable cells

was depressed in the same TCM conc. range as that required for cell growth inhibition of cell RNA synthesis. There was a marked suppression of uridine incorporation into 28S RNA, a lesser effect on 18S RNA, little or no effect on 4S RNA and a very small accumulation of RNA's in the 30-45S range. Ultrastructural changes consisted only of nucleolar alteration with dispersion of constituents, but without notable rearrangement or quantitative change in the components. This contrasted sharply to nucleolar response to treatment of AMV leukemia myeloblasts or other cells with actinomycin D, but the changes were similar to those in other cells induced by treatment with ethionine or adenosine.

70-1578 ANTIGENIC LOSS IN A TRANSPLANTABLE, CHEMICALLY INDUCED LEUKEMIA OF C57BL/6 MICE. (E.) Rubin, D. J. (NCI, Bethesda, Md.), H. R. Colten, R. Borsos and H. J. Rapp. J. Nat. Cancer Inst. 44(4):975-979, 1970.

In C57BL/6 mice, cell surface antigens of transplantable EL4 leukemia (induced by 7,12-dimethylbenzanthracene) and Friend virus- and Rauscher virus-induced leukemias were studied by the C_I fixation and transfer test. EL4 cells lacked at least 1 antigen found on the surfaces of normal lymphoid cells and cells of the 2 virus-induced leukemias. It is concluded that the absence of "normal" antigen on EL4 cells precludes their use in immunological studies of tumor-specific membrane antigens.

70-1579 SUPPRESSION OF RAUSCHER VIRUS-INDUCED LEUKEMIA BY L-ASPARAGINASE. (E.) Campbell, W. F. (Indiana U. Med. Ctr., Indianapolis) and A. S. Levine. Life Sci. 8, Pt. 2(20): 1033-1040, 1969.

Mice inoc. neonatally with Rauscher leukemia virus (RLV) were treated with L-asparaginase (L-A) from Escherichia coli, either as a single dose 1 hour before RLV inj. (15 I.U.), or in 7 doses (5 I.U. each) from day 2-20 after virus inj. Some mice were treated with L-asparagine or L-aspartic acid (each 10 µmoles) and some were treated with L-A and L-asparagine combined. Treatment with L-A suppressed splenomegaly and prolonged the survival time, but did not inhibit viremia (all mice eventually died with leukemic splenomegaly). Pretreatment with L-A did not protect the mice against leukemia development. Admin. of L-asparagine partially suppressed the leukemic process and did not inhibit the anti-leukemic effects of L-A. Aspartic acid had no antileukemic activity.

70-1580 RAUSCHER VIRAL LEUKEMOGENESIS IN BALB/c MICE TREATED WITH RABBIT ANTI-MOUSE THYMOCYTE SERUM. (E.) Siegel, B. V. (U. Oregon Med. Sch., Portland) and J. I. Morton. J. Nat. Cancer Inst. 44(3):573-579, 1970.

Splenomegaly was delayed in 6-8-week-old, Rauscher leukemia virus (RLV)-infected BALB/c mice by multiple inj. of rabbit antimouse thymocyte serum (ATS). A regimen of 9 inj. of ATS was toxic to RLV-inoc. animals, but a program of 6 inj., 3 before and 3 after viral inoc., delayed the onset of deaths of infected mice by 1-2 weeks and gave a significantly increased survival rate. A single inj. of 0.5 ml ATS admin. 2 days before RLV infection did not significantly affect leukemogenesis. Multiple ATS inj. produced more immunodepression (measured by spleen plaque formation following sheep RBC immunization) than a single inj.; 1, 6 and 9 inj. of ATS resulted in depression to the extent of 40, 22 and 14%, resp., of the antibody response obtained with controls. It is suggested that the influence of ATS on RLV leukemogenesis is due to changes induced in numbers and properties of viral target cells more than to changes in host immune capacity.

70-1581 INVESTIGATIONS OF SURVIVAL PROPERTIES OF AIR-BORNE MURINE LEUKEMIA VIRUS. (E.) Larson, E. W. (Fort Detrick, Frederick, Md.), G. J. Spahn, R. L. Peters and R. J. Huebner. *J. Nat. Cancer Inst.* 44(4):937-941, 1970.

Rauscher leukemia virus aerosols were generated in a static cloud chamber under conditions similar to those in animal colonies. More than 99% of the virus was inactivated in the process of aerosolization and equilibration with the environment; after this, the virus aerosols were relatively stable, with an inactivation rate of about 1%/min. Efforts to recover the virus from air samples collected from infected mouse colonies were not successful. The feasibility of using conventional aero-biological methods in the study of mouse leukemia virus is discussed.

70-1582 IMMUNOCOMPETENCE OF LEUKEMIC MURINE LYMPHOBLASTS: ULTRASTRUCTURE, VIRUS AND GLOBULIN PRODUCTION. (E.) Trujillo, J. M. (M. D. Anderson Hosp. Tumor Inst., Houston, Tex.), M. J. Ahearn, R. J. Pienta, C. Gott and J. G. Sinkovics. *Cancer Res.* 30(2):540-545, 1970.

Immunofluorescence studies of mouse lymphoma cell line 818 (obtained from mice inoc. with Rauscher leukemia virus) with antisera specific for the 5 major classes of mouse immunoglobulins showed that these cells could produce immunoglobulins γ_1 and γ_2a . The presence of Rauscher viral antigens in the same cell line was demonstrated in similar studies with specific monkey and rabbit anti-Rauscher sera and confirmed by electron microscopy. It is indicated that this cell line has the capacity both to produce immunoglobulins and to carry or replicate a leukemogenic virus at the same time. The importance of these findings with regard to the known association between immunity disorders and RES neoplasms is discussed.

70-1583 VIRAL RNA-DEPENDENT DNA POLYMERASE IN VIRIONS OF RNA TUMOUR VIRUSES. (E.) Baltimore, D. (Massachusetts Inst. Technol., Cambridge). *Nature (London)* 226(5252):1209-1211, 1970.

Data are presented which demonstrate that an RNA-dependent DNA polymerase is present in the virions of 2 RNA tumor viruses, the Rauscher mouse leukemia virus (RLV) and the Rous sarcoma virus (RSV). After isopycnic centrifugation, RLV displayed polymerase activity at the position of the visible band of virions and the reaction product displayed properties of DNA when subjected to various treatments. RNA was demonstrated as the template for the virion DNA polymerase by the sensitivity of the reaction to ribonuclease. RLV polymerase incorporated only deoxyribonucleotides, in contrast to vesicular stomatitis virus, which incorporated only ribonucleotides. When assayed for DNA polymerase activity, a preparation of the Prague strain of RSV incorporated label, and activity was severely reduced when either Mg or deoxyadenosine triphosphate were omitted from the reaction mixture. It is thought that RNA-dependent DNA polymerase is a constituent of all RNA tumor viruses; this feature is important in the understanding of carcinogenesis by RNA viruses and genetic transcription. It is suggested that the classical process of information transfer from DNA to RNA can be inverted.

70-1584 CHARACTERISTICS OF LONG-TERM MARMOSET CELL CULTURES SPONTANEOUSLY ALTERED OR TRANSFORMED BY ROUS SARCOMA VIRUS. (E.) Marczyńska, B. (Presbyterian-St. Luke's Hosp., Chicago, Ill.), G. Treu-Sarnat and F. Deinhardt. *J. Nat. Cancer Inst.* 44(3):545-572, 1970.

Kidney cells from an adult male marmoset (*Saguinus fuscicollis*) were established in cell culture and exposed to Schmidt-Ruppin Rous sarcoma virus (SR-RSV) at different passage levels. In 5 independent series, only 1 culture of 6 inoc. cell lines was transformed by SR-RSV, when cells were inoc. in the G₁ phase. The transformed cells formed foci of sarcoma cells in culture and gave rise to a tumor after transplantation into the original kidney-donor animal, but did not grow as microtumors after implantation into hamster cheek pouches. No infectious virus was recovered from cells transformed *in vitro*, even after cocultivation with chick embryo fibroblasts, but infectious SR-RSV was recovered after cells grew as a sarcoma in the autologous animal. Of 7 uninfected cell lines and 5 lines inoc. with SR-RSV but not transformed, 5 permanent cell strains were established and maintained *in vitro* for 4 yr. Chromosomal changes observed included a reduced number of diploid cells with the appearance of such chromosomal abnormalities as rings, dicentric and extra-large size. Cells did not grow in soft agar or induce tumors when transplanted to

hamster cheek pouches or the original kidney donor. The use of the cell culture lines or strains for the production of viral vaccines is suggested.

70-1585 TUMOR INDUCTION IN ADULT RATS BY ROUS SARCOMA VIRUS OF CHICKENS. (Rus.)

Kuznetsova, N. N. (Gamalei Inst. Epidemiol. Microbiol., Moscow) and V. Ia. Shevliagin. Vop. Onkol. 15(8):40-47, 1969.

Cellular suspensions of the Schmidt-Ruppin (RSV-SR) or Carr-Zilber (RSV-CZ) strains of Rouse sarcoma virus (containing 10^5 - 10^7 tumor-inducing units/0.1 ml as determined in 14-day-old chickens), were inj. i.m. into 4-6-mo.-old rats. In Wistar rats, 1 or 5 inj. (5 ml each) of RSV-CZ induced early tumors (which disappeared after 2 weeks) in 2/10 and 9/30 rats, resp. In August rats, 4 inj. of RSV-CZ (each 4 ml) induced a tumor in only 1/60 rats. In several groups of Wistar rats inj. with different doses of RSV-SR, the tumor incidence increased according to the total virus dosage, from 43.3% (11/32 rats) after a single 1-ml inj., to 61.1% (44/89 rats) after 4 inj. (each 4 ml). In these rats, the tumors developed after 15 days-8 mo. (usually 1-2 mo.) and sometimes metastasized to the abdominal cavity. In August rats, 4 inj. of RSV-SR (each 4 ml) induced a tumor in only 1/72, while 1 inj. (4 ml) induced no tumors among 10 rats. A majority of the rats in each virus-inj. group survived to the end of the experiments (usually 7-12 mo.). Latent periods were shorter in rats admin. several virus inj. (at 5-7-day intervals) than in rats receiving only 1 virus inj. The early tumors and some of the later-developing tumors were polymorphocellular sarcomas; the remainder of the late tumors were fibrosarcomas. The early tumors grew rapidly and sometimes metastasized to the abdominal cavity; the late tumors grew slowly and did not metastasize. A rat karyotype was noted in 18 of the primary tumors. Multiple chromosomal aberrations (including aneuploidy and marker chromosomes) were seen in 2/2 tumors examined.

70-1586 IMMUNOLOGICAL DETERMINANTS OF AVIAN SARCOMA VIRUSES: PRESENCE OF GROUP-SPECIFIC ANTIBODIES IN FOWL SERA DEMONSTRATED BY COMPLEMENT-FIXATION INHIBITION TEST. (E.)

Rabotti, G. F. (Coll. France Lab. Exp. Med., Paris) and E. Blackham. J. Nat. Cancer Inst. 44(5):985-991, 1970.

Group-specific antibodies in sera of chickens and turkeys immunized with the Rous sarcoma virus (RSV) were detected by a complement-fixation inhibition test. The antibodies were specific for antigen preparations of the avian leukosis complex, and cross-reacted with all antigens studied with the characteristics of group-specific antibodies. Antigens examined included cultured chick embryo cells infected

with 3 strains of RSV (Bryan high-titer [BH-RSV], Schmidt-Ruppin [SR-RSV] and Harris) and a strain of avian lymphomatosis RPL12, tumors induced in chickens, turkeys and Japanese quail with BH-RSV and SR-RSV, and hamster tumors induced by SR-RSV.

70-1587 INDUCTION OF TUMORS IN HAMSTERS BY RAT ROUS SARCOMA RBI, PRODUCING CHICK

SARCOMA VIRUS. 1. CONTINUOUS PRODUCTION OF VIRUS ONCOGENIC FOR CHICKS BY HAMSTER SARCOMA CELLS. (E.) Svec, J. (Cancer Res. Inst., Bratislava, Czechoslovakia), F. Svec, D. Šimkovič and V. Thurzo. J. Nat. Cancer Inst. 44(3):521-532, 1970.

Sarcomas were induced in hamsters by RBI rat sarcoma cells, which also produced Rous sarcoma virus pathogenic for chickens. A successful double heteroinduction (chicken-rat, rat-hamster) occurred, in spite of the low virus content in the RBI sarcomas. The hamster sarcoma cells (designated RBH), and virus preparations isolated from them, induced sarcomas in chickens. RBH cells grown in tissue culture (designated RBH_{tc}) released a virus infectious to chickens. Chromosomal analysis of RBH and RBH_{tc} confirmed their hamster origin.

70-1588 DEMONSTRATION OF THE ACTIVITY OF SEVERAL DEHYDROGENASES IN AVIAN FIBROBLASTS TRANSFORMED IN VITRO BY ROUS SARCOMA VIRUS. (Fr.) Francois, D. (Coll. France, Lab. Exp. Med., Paris). J. Gen. Virol. 6(2):187-199, 1970.

In chick embryo fibroblasts cultured in vitro and infected with a suspension of Schmidt-Ruppin strain Rous sarcoma virus (RSV; 0.1 ml/5 ml medium; titer = 10^5 - 10^7 FFU/ml), transformed cells showed significantly increased activities of lactic, isocitric, succinic, malic and glucose-6-phosphate dehydrogenases. Reactive sites were more numerous and stained more intensely than those seen in either uninfected fibroblasts or fibroblasts infected with 2 other viruses of the avian leukosis group (RAV-1, RAV-2). Mitochondria in the RSV-transformed cells were more rounded than those in control cultures, but showed no electron microscopic changes which would indicate increased permeability with respect to the reagents employed. It is concluded that the increased glycolysis of the transformed cells was not accompanied by any weakening of the enzymatic respiratory systems.

70-1589 IMMUNOTHERAPY OF PRIMARY MOLONEY SARCOMA-VIRUS-INDUCED TUMORS. (E.)

Fefer, A. (U. Washington, Seattle). Int. J. Cancer 5(3):327-337, 1970.

In adult BALB/c mice inoc. with Moloney sarcoma virus (MSV), 90% (84/94) of tumors underwent

immunologically-mediated regression; 97% and 80% of tumor-bearing mice treated with 180 or 115 mg/kg of cyclophosphamide (C; admin. i.p.), resp., died with progressively-growing tumors. In adult BALB/c mice with primary tumors treated with C and inj. with BALB/c spleen cells, 80/85 tumors treated with cells from mice immunized with MSV completely regressed, but only 6/92 tumors regressed after treatment with normal or non-specifically immunized cells, or with non-viable immune cells. The antitumor effect of C was not essential for the immunotherapeutic effect of the cells. With allogeneic spleen cells, those from DBA mice were effective only if specifically pre-immunized with MSV or BALB/c Moloney sarcoma cells. Animals treated with cells from C57Bl/6 donors immunized with MSV died free of tumor with graft-versus-host disease, but those given non-immunized cells died of graft-versus-host disease with tumor. Specific serotherapy was only moderately effective, as compared to cellular therapy. In studies with γ -globulin allotype as a marker for donor cells, results indicated that immune cells may have to persist in the host for some time to be effective against the tumor.

70-1590 STUDIES ON THE ENZYMOLOGY OF THE RHABDOMYOSARCOMA INDUCED BY THE MURINE SARCOMA VIRUS (MOLONEY). (E.) Ebert, P. S. (NCI, Bethesda, Md.), M. A. Chirigos and S. P. Chan. Cancer Res. 30(4):960-965, 1970.

In adult mice with a Moloney sarcoma virus-induced rhabdomyosarcoma, protein, water, RNA and DNA conc. increased with tumor growth, while actomyosin-free Mg^{2+} -activated ATPase and lactate dehydrogenase (LDH) activity decreased. Glucose-6-phosphate dehydrogenase and 6-phosphogluconate dehydrogenase activities increased markedly and continued to increase during spontaneous tumor regression. Significantly increased activity remained when the tumor was undetectable by palpation. Tumor levels of acid phosphatase were almost 3-fold that of normal muscle. Reduced LDH activity and low lactate accumulation in the tumor (compared to normal muscle) suggested an unusual pattern of nicotine adenine dinucleotide metabolism in comparison to other tumors. High titers of LDH virus were found both in tumors and inoculum.

70-1591 SARCOMA-SPECIFIC ANTIGENS: DETECTION BY COMPLEMENT FIXATION WITH SERUM FROM SARCOMA PATIENTS. (E.) Eilber, F. R. (NCI, Bethesda, Md.) and D. L. Morton. J. Nat. Cancer Inst. 44(3):651-656, 1970.

The complement-fixation studies of the distribution of antibodies to the SA1 (human liposarcoma cell line) antigen in sera of pts. with various malignancies were made. Sera from 29/31 (92%) pts. with skeletal or soft tissue sarcomas showed detectable antibody to a titer greater

than 1:8. Incidences and mean titer of antibody in sarcoma pts. were significantly greater than those of normal blood donors. Pts. with malignant melanomas and carcinomas of the lung, head and neck, colon, breast and cervix did not show a significantly different incidence or mean titer of antibody from normal blood donors. Additional cell lines (derived from osteosarcoma and fibrosarcoma) gave similar results when tested with the same sera as used for the SA1 antigen. The incidence of antibody to SA1 sarcoma antigen was 62/65 (95%) in sarcoma pts., 25/37 (67%) in family members of sarcoma pts., and 10/40 (25%) in normal blood donors. It is suggested that human sarcomas are associated with an infectious agent that can produce unrecognized infections in healthy associates of sarcoma pts.

70-1592 VIRUS PARTICLES IN TISSUE CULTURES OF A HUMAN LIPOSARCOMA. (E.) Hall, W. T. (Electro-Nucleonics Labs., Inc., Bethesda, Md.), D. L. Morton and R. A. Malmgren. J. Nat. Cancer Inst. 44(3):507-513, 1970.

Cultures of cells from a malignant pleural effusion of a 60-yr.-old man with a liposarcoma, contained multilayered foci of tightly-packed, lipid-containing cells which developed by day 57. Virus particles were found budding into intracytoplasmic vesicles of cells in all foci observed, but none were observed in nonfocal cells. Particles did not bud from the plasma membrane, but mature extracellular virions were noted. The particles (about 85-100 m μ diameter) were morphologically similar to Type C viruses of various animal tumors. Infectivity of the particles could not be demonstrated.

70-1593 BIOACTIVITY AND VIRIONS IN THE BLOOD OF MICE WITH MAMMARY TUMOR VIRUS. (E.) Moore, D. H. (Inst. Med. Res., Camden, N. J.), N. H. Sarkar and J. Charney. J. Nat. Cancer Inst. 44(4):965-973, 1970.

Nodule development in hormone-stimulated BALB/c female mice was used to assay blood fractions in a study of the mammary tumor virus (MTV) in the blood. Blood cells had plasma from strains RIII/Haag, A/Bi and BALB/c f. C3H/Crgl yielded endpoints (bioactivity) at dilutions no greater than 10^{-2} , compared to 10^{-6} to 10^{-7} for RIII milk. The titer was less in plasma than in the cellular fraction. Lysed cells had bioactivity in the stroma, but not in the Hb fraction. B particles (MTV virions) were found in blood after extraction and conc.; the conc. of these particles and bioactivity varied between mouse strains and between individual mice of the same strain. Freezing and thawing markedly reduced the bioactivity of milk, bone marrow and blood cells.

70-1594 ULTRASTRUCTURAL AND QUANTITATIVE STUDIES OF MAMMARY TUMOR VIRUS

PRODUCTION IN CULTURED MOUSE MAMMARY TUMOR CELLS. (E.) Kramarsky, B. (Inst. Med. Res., Camden, N. J.), E. Y. Lasfargues and D. H. Moore. Cancer Res. 30(4):1102-1108, 1970.

Budding mammary tumor virus (MTV) was compared with leukemia virus by use of a whole-cell-mounting method that allowed visualization of ultrastructural detail, including cores and surface spikes of budding virions. Binding of specific antibody to budding MTV virions was directly seen without use of conjugated antibody. Antibody was bound only to the virus bud and not to other regions of the cell membrane. Binding was not seen in control sera. Virus production in infected cells was assayed by the same method. The MMT/R-5 cell line had a higher ratio of producing cells than the MMT (Sykes) cell line (derived from a spontaneous mammary tumor), from which it was obtained by alternate in vivo-in vitro passage in Amsterdam rats. With aging of cultures, MMT productivity approached zero, but that of MMT/R-5 cells increased.

70-1595 IMMUNOLOGY OF THE MOUSE MAMMARY TUMOR VIRUS: COMPARISON OF THE ANTIGENICITY OF MAMMARY TUMOR VIRUS OBTAINED FROM SEVERAL STRAINS OF MICE. (E.) Blair, P. B. (U. California Cancer Res. Genet. Lab., Berkeley). Cancer Res. 30(3):625-631, 1970.

Antigenic properties of mammary tumor virus (MTV) strains derived from various mice were detected by use of the MTV antigen in immuno-diffusion studies using rabbit antisera. Cross-reactivity was shown in samples of a soluble MTV antigen from virus originally derived from GR, DBA, WILD, RIII, A, C3H or C3Hf mice. A similar cross-reacting antigenicity was found among preparations of MTV B-particle preparations. MTV from C3Hf mice and from wild house mice lacked at least 1 antigenic component possessed by MTV from other sources, such as MTV of DBA or C3H origin. The significance of these antigenic similarities and differences is discussed.

70-1596 IMMUNOLOGY OF SPONTANEOUS MAMMARY CARCINOMAS IN MICE: IMMUNOGENICITY OF MAMMARY TUMOR VIRUS-CONTAINING TISSUES IN MAMMARY TUMOR VIRUS-FREE C3H/2 HOSTS. (E.) Lavrin, D. H. (U. Illinois Med. Ctr., Chicago). Cancer Res. 30(4):1156-1162, 1970.

The immunogenicity of isogeneic mammary tissue of mammary tumor virus (MTV)-containing C3H/2 mice, hyperplastic alveolar nodules and mammary tumors in MTV-free C3H/2 mice was studied. Specimens of C3H normal mammary tissue and two C3H hyperplastic alveolar nodules grew poorly, or not at all, in adult C3H/2 hosts and gave good protection against further C3H tumor challenge. These tissues did not give protection to immature C3H/2 hosts, and a significant reduction in response was seen in aged hosts. A similar

strong reactivity to an MTV-infected C3H/2 mammary tumor by MTV-free mice was seen, but not by mice infected with the virus. It is concluded that MTV is important in the immunogenicity of normal, pre-neoplastic and neoplastic mammary tissues.

70-1597 STIMULATION OF MAMMARY TUMOR VIRUS PRODUCTION IN A MOUSE MAMMARY TUMOR CELL LINE. (E.) Lasfargues, E. Y. (Inst. Med. Res., Camden, N. J.), B. Kramarsky, N. H. Sarkar, J. C. Lasfargues, N. Pillsbury and D. H. Moore. Cancer Res. 30(4):1109-1117, 1970.

In a mouse mammary tumor cell line (MMT) that was alternately passaged through newborn mice (strains C57BL, Af and A) or newborn rats (Amsterdam/IMR) and tissue culture, the passage of MMT cells into mice and back to tissue culture stimulated a 4-fold increase of Type B particle production by the cell line, but was subject to variations in successive subcultures. When passaged into rats, virus production increased 25-30-fold; virion budding remained constant and tumor-inducing capabilities were high through multiple subcultures. The greater stability in pH and stable growth rate of rat-passaged cells, suggested the possibility of production in tissue culture of a mammary tumor virus of greater purity and reliability than that obtained from milk or tumor extracts.

70-1598 A VIRUS (RMTDV) DERIVED FROM CHEMICALLY INDUCED RAT MAMMARY TUMORS. I. ISOLATION AND GENERAL CHARACTERISTICS. (E.) Bergs, V. V. (U. Miami Sch. Med., Fla.), M. Bergs and H. C. Chopra. J. Nat. Cancer Inst. 44(4):913-922, 1970.

Isolation of a rat mammary tumor-derived virus (RMTDV) in a line of embryo cells (REL) from 1/3 Lewis and 1/3 Sprague-Dawley rat mammary carcinomas induced by 7,12-dimethylbenzanthracene (20 mg, p.o.) and their primary cell cultures. A cell line (RMTL-8) from another Sprague-Dawley rat mammary tumor was also found infected with RMTDV. Typical cytopathic effects were produced by the virus in REL cell cultures. RMTDV was filterable through Millipore membranes of 220 (but not 110) mμ porosity, did not agglutinate guinea pig RBC and was completely inactivated by lipid solvents, a pH of 2.3 and 11.9 and a temperature of 56° C. Antisera specific to Kilham's rat virus, polyoma virus, mouse hepatitis virus, Rauscher mouse leukemia virus and the 9H virus did not neutralize RMTDV, but several sera from normal Lewis, Wistar-Furth and Sprague-Dawley rats exhibited low or moderate RMTDV neutralizing activity. RMTDV had morphological features identical to C-type virus particles, and extracellular mature particles were 90-100 mμ in diameter. When inj. at birth with 10⁴-10⁵ TCID₅₀ of RMTDV, 17/330 (5.2%) of Sprague-Dawley rats developed lymphoid leukemia

after a latent period of 5.5-11.0 mo., and 12 developed coagulative liver necrosis in 2-11 mo. In one animal there was both a lymphoblastic lymphoma and liver necrosis. The etiological relationship of RMTDV to liver necrosis is suggested.

70-1599 ATTEMPTS TO DETECT NODULE-INDUCING VIRUS IN STRAIN RIII MICE. (E.)

Smith, G. H. (NCI, Bethesda, Md.), H. B. Andervont and T. B. Dunn. J. Nat. Cancer Inst. 44(3):657-671, 1970.

High-mammary tumor strain RIII mice, free of the mammary tumor virus (MTV) and designated RBR, were studied to see if they carried an agent similar to nodule-inducing virus (NIV), which is responsible for the appearance of spontaneous mammary tumors in C3Hf mice. After hybridization experiments were done between these mice and those of strains BALB/c (NIV⁻) and C3Hf (NIV⁺), mammary tumors that developed in these hybrids and in MTV-free RBR females were studied by electron microscopy to detect the presence of NIV. It is concluded that the RIII mice did not have an MTV variant similar to the NIV of C3Hf mice. A relationship between the many intracisternal type A particles noted in their tumors and in tumors of reciprocal RBR x BALB/c hybrids and MTV gene action is suggested.

70-1600 STUDIES ON THE RELATIONSHIP OF VIRUSES TO THE ORIGIN OF HUMAN BREAST CANCER.

II. VIRUSLIKE PARTICLES IN HUMAN BREAST TUMORS. (E.) Seman, G. (U. Texas M. D. Anderson Hosp., Tumor Inst., Houston), B. Myers, W. C. Williams, H. S. Gallager and L. Dmochowski. Texas Rep. Biol. Med. 27(3):839-866, 1969.

Electron microscopic examination of biopsies from 33 breast tumors (1 comedocarcinoma, 7 stellate carcinomas, 1 each of mucinous, medullary or mixed patterns and 22 unspecified), 1 fibroadenoma, and 3 postradiated and postexcisional breast specimens were done, and mammary tumor virus-like particles were found in 9/34 tumor specimens (including the fibroadenoma), while particles resembling Type C mouse leukemia virus particles were found in 4/34. Budding resembling formation of virus particles was found in 2 cases. Particles resembling small virus particles (300-500 Å) were seen in 10/34 tumor specimens, and isolated herpes-type particles were found in 2 specimens. No particles resembling virus particles could be found in the 3 postradiated and postexcisional breast specimens. No connection could be established between the histologic type of breast cancer and the presence of virus-like particles. Small virus-like particles were seen in 4 different passages of tissue culture derived from a pt. with breast carcinoma; occasional particles resembling Type B and Type C particles were found in 2 passages of tissue culture of the same tumor.

70-1601 HISTOPATHOLOGY OF TUMORS AND CULTIVATION OF TUMOR CELLS DERIVED FROM SIMIAN ADENOVIRUS SV20-INFECTED HAMSTERS. (E.)

Schoentag, R. A. (Holloman Air Force Base Aeromed. Res. Lab., N. Mex.), C. K. Y. Fong and G. D. Hsiung. Cancer Res. 30(3):863-870, 1970.

The histopathological patterns of tumors in hamsters, induced either by inoc. of SV20 virus suspension, transplantation of SV20 tumor tissues or inoc. with cultivated SV20 tumor cells were similar. The tumors were always located at the inj. site and consisted essentially of a sheet of uniform undifferentiated cells. Metastases were uncommon, but were seen in brown fat, liver, lungs, salivary glands and skeletal muscle, and were unrelated to materials used for tumor induction. Cultivated SV20 hamster tumor cells were fused successfully with monkey kidney cells in the presence of a pseudomyxovirus, foamy virus type 1. Bridge formations occurred between nuclei of monkey kidney cells and hamster tumor cells, but SV20 virus-induced inclusions were not observed in monkey cells in close contact with hamster tumor cells.

70-1602 PRODUCTIVE AND ABORTIVE GROWTH OF AN ONCOGENIC SIMIAN ADENOVIRUS SV20 IN CULTURED CELLS. (E.)

Fong, C. K. Y. (Putnam Mem. Hosp. Inst. Med. Res., Bennington, Vt.) and G. D. Hsiung. Cancer Res. 30(3):855-862, 1970.

An oncogenic simian adenovirus, SV20, was grown in rhesus monkey (RhMK) and hamster kidney (HamK) cell cultures. The rate of absorption of SV20 in both systems was slow, but increased with time from 30 min. to 6 hours. From 3-8 times more cell-associated virus in RhMK cells was seen during the initial 6 hours of infection. Infected monkey cells showed a complete growth cycle of SV20, including sequential nuclear alterations, production of T antigen, viral antigen and infectious virus. SV20 induced an abortive infection in hamster cells. T antigen and eosinophilic inclusions were shown to be 2 separate entities in infected hamster cells, but there was no infectious virus or viral antigen in the hamster cell system. DNA synthesis was markedly stimulated in SV20-infected HamK cells.

70-1603 RELATIONSHIP BETWEEN IMMUNOLOGIC MATURATION AND VIRAL ONCOGENESIS IN HAMSTERS. (E.)

Friedman, H. (Albert Einstein Med. Ctr., Philadelphia, Pa.) and H. Goldner. J. Nat. Cancer Inst. 44(4):809-817, 1970.

Hamsters were inoc. at birth with either SV40 or adenovirus 12; the virus-infected animals were challenged with sheep RBC when 1-6 weeks old, and the number of antibody plaque-forming cells (PFC) was determined. When immunized at 1 week of age, normal controls developed few splenic antibody plaques; immunoresponsiveness increased quickly, and by weeks 3-4 large

quantities of antibody-forming cells developed after admin. of sheep RBC. There was little effect on the capability of hamsters inoc. at birth with either virus to respond to sheep RBC at 3-4 weeks of age. The number of PFC was moderately depressed in virus-infected animals challenged at weeks 1-2, in comparison to controls. The animal's age at the time of infection was directly related to susceptibility to tumorigenesis. When inoc. before 3 days of age, more than 95% of hamsters developed tumors between 90-150 days of age. About 20-25% of animals developed tumors when infected with either virus at 1 or 2 weeks of age; no tumors developed in those infected when 3 weeks old or older.

70-1604 TWO DISTINCT TYPES OF SV40-TRANSFORMED HUMAN AMNION CELLS. (E.) Gaffney, E. V. (Pennsylvania State U., University Park), L. Ramos and J. Fogh. Cancer Res. 30(3):871-879, 1970.

When human epithelial amnion cells were infected in primary culture with SV40, they transformed and produced 2 morphologically different cells (T and R). T foci appeared 17 days after infection, and R foci appeared 28 days after infection; the ratio of R to T cell foci increased when older amnion cultures were infected. While T cells were easily subcultured by usual trypsinization methods, the more slowly dividing R cells were resistant to treatment with enzymes and chelating agents and required special subcultivation methods. Cultures of both cell types produced SV40, but R cell cultures had higher virus titers and contained more virus-producing cells. Chromosome numbers of R cells were near tetraploid in the early stages of cultivation, but T cells remained in the diploid range for longer periods. R cells produced more growth than T cells in the cheek pouch of weanling golden Syrian hamsters conditioned with cortisone acetate (5 mg, s.c.). In both R and T cultures, 100% of the cells contained T antigen. It is suggested that the amount of R-cell transformation was related to formation of a population in older, uninfected primary cultures with an abnormal genetic constitution.

70-1605 COMPLEMENT-FIXING SV40 ANTIBODIES IN YOUNG CHILDREN WITH TUMORS. (It.) Benso, L. (U. Turin Pediat. Clin., Italy), M. R. Brunet and P. Iudicello. Minerva Pediat. 22(9):428-432, 1970.

Anti-SV40 complement-fixing antibodies were found in 17/23 (73.9%) children, 12 with leukemias and 11 with solid tumors; the max. antibody titer was 1:32 (mean 1:11.5). Antibodies were found in 9/12 (75%) with leukemia, with a max. titer of 1:32 (mean 1:11.8). Of the children with solid tumors (3 lymphosarcomas, 3 unspecified brain tumors, 2 reticulum cell

sarcomas, 1 Wilms' tumor, 1 hepatoma, 1 osteosarcoma), 8/11 (72.7%) showed antibodies, with a max. titer of 1:32 (mean 1:11.2). All pts. had received the Sabin live polio vaccine. Examination of 32 healthy controls, matched for age and sex, revealed antibodies in 96.8%, and a mean titer of 1:58.4.

70-1606 DIFFERENCES OF ANTIGENICITY OF HAMSTER FIBROBLASTS TRANSFORMED BY SV40 AND THEN CLONED (TSV5C12), DEPENDING UPON WHETHER THEY ARE MAINTAINED IN TISSUE CULTURE OR PROPAGATED IN THE ANIMAL. (Fr.) De Vaux-St-Cyr, C. (Sci. Res. Inst. Cancer, Villejuif, France). C. R. Acad. Sci. [D] Paris 269(12):1148-1150, 1969.

The TSV5C12 cell line, derived from a tumor induced in a neonatal Syrian hamster by inj. of SV40 and cultured *in vitro*, contained 3 tumor-specific antigens, localized in the cytoplasm of the transformed cells and particularly in the perinuclear zone. When the culture was inj. s.c. into other Syrian hamsters, 3/3 antigens were demonstrable in the sera of tumor-bearing hosts, but none were demonstrable in tumor tissue extracts or in cell cultures derived from these hosts. However, all 3 antigens reappeared in such *in vitro* cultures, about 1 week after they were begun. No explanation for this phenomenon is offered.

70-1607 TRANSFORMATION OF HUMAN DIPLOID CELLS BY THE SV40 VIRUS. (Cz.) Kutinová, L. (Res. Inst. Immun., Prague), M. Macek, V. Vonkš, K. Smetana and H. Závadová. Cesk. Epidem. 18(1):1-8, 1969.

In SV40-transformed LEP-12 human diploid cell cultures, growth was stimulated on day 34 of cultivation (passage 6), signs of loss of contact inhibition were present on day 52 (passage 9), and large, rounded cells appeared on day 150. The transformation was accompanied by a loss of the diploid chromosome number (diploid mitoses disappeared in passage 23), a decrease in the proportion of sex chromatin-positive cells (from 21% or more in control cultures, to 2.8-4.6%), the appearance of numerous chromosomal aberrations (fragmentation, acentrics, dicentrics, rings, exchanges and endomitotic figures), and a significant increase in the nucleolar index. The content of infectious SV40 decreased gradually during successive passages. The T antigen of SV40 was detected in transformed cells by complement fixation and indirect immunofluorescence methods.

70-1608 QUANTITATIVE ASPECTS OF THYMIDINE UPTAKE INTO THE ACID-SOLUBLE POOL OF NORMAL AND POLYOMA-TRANSFORMED HAMSTER CELLS. (E.) Hare, J. D. (U. Rochester Sch. Med. Dent., N. Y.). Cancer Res. 30(3):684-691, 1970.

Hamster tumor cells transformed by polyoma virus had a 4-fold increased capacity to incorporate thymidine as phosphorylated products into an acid-soluble pool when compared to normal hamster embryo cells. This uptake capacity was correlated with a 5-10-fold higher activity of thymidine kinase in the tumor cell lines. The uptake was not inhibited by uridine, but strongly inhibited by 5-iodo-2'-deoxyuridine and partially inhibited by deoxyuridine.

70-1609 THE ROLE OF THE DERMIS IN THE INDUCTION OF NEOPLASIA BY SHOPE PAPILLOMA VIRUS.

(E.) Breedis, C. (U. Pennsylvania Sch. Med., Philadelphia) and J. W. Kreider. Cancer Res. 30(4):974-979, 1970.

The role of the dermis in the induction of neoplasia in autografts of rabbit skin infected with Shope papilloma virus (SPV) was studied. Skin fragments were dissociated into epidermal and dermal components with trypsin, and combinations of epidermis (both in cell suspensions and sheets) and viable or frozen dermis were SPV-infected and grafted to the lumbodorsal fascia or the panniculus carnosus. Transplants of epidermis infected with SPV became papillomatous; no dependence on the physical presence of dermis or on transitory dermal influences was noted. Papillomas that developed in epidermis transplants alone were representative of the typical morphology of this tumor and identical with controls. Tumors derived from epidermal-dermal recombinants were often larger than those developing from epidermis alone. It is concluded that little or no dermis is required for the development of typical Shope papillomas from SPV-infected epidermal cells.

70-1610 ISOLATION OF DNA FROM SHOPE FIBROMA VIRUS AND SOME OF ITS PROPERTIES.

(Fr.) Jacquemont, B. (INSERM Inst. Virol., Lyon, France), P. Precosta and D. Gautheron. Bull. Soc. Chim. Biol. (Paris) 51(2):225-244, 1969.

Purified Shope fibroma virus consisted primarily of proteins, with a DNA content of 5.3% and an insignificant RNA content of 0.4%. Like cellular DNA (calf thymus; rabbit skin, liver, and kidney), the viral DNA showed a bicatenoid structure. The hyperchromic effect at 260 mμ in the presence of formol (1%; at 100° C x 10 min.) was 30%, as compared to 34% for cellular DNA; the fusion curve showed the same shape as that of cellular DNA. Fusion temperature was 83.8° C, as compared to 86.3° C for cellular DNA. Density at equilibrium in cesium chloride was 1.696 g/ml, as compared to 1.700 g/ml for cellular DNA (rabbit liver), with a combined guanine + cytosine content of 36 mole % and 42 mole %, resp. In contrast to DNA derived from other pox viruses, Shope fibroma virus DNA was not infectious in cell culture.

70-1611 REPLICATION OF HERPES SIMPLEX VIRUS IN CULTURES OF PHYTOHEMAGGLUTININ-STIMULATED HUMAN LYMPHOCYTES. (E.) Bouroncle, B. A. (Ohio State U., Columbus), K. P. Clausen and E. M. Darner. J. Nat. Cancer Inst. 44(5):1065-1078, 1970.

Replication of herpes simplex virus (HSV) in phytohemagglutinin (PHA)-stimulated lymphocytes was studied by electron microscopy and infectivity titer. Max. infectivity titers occurred in 48 hours, and unstimulated lymphocytes showed only a slight increase in viral infectivity titers. New virus was first seen in infected cultures 24 hours after inoc., and at 48 hours almost all viable cells contained virus in different stages of proliferation. There was no evidence of replication in non-transformed lymphocytes. It is suggested that cultures of PHA-stimulated normal human lymphocytes can be used in identification of unknown human viruses and may be valuable for isolation of possible human lymphotropic viruses.

70-1612 LEUKAEMIA AND CYTOMEGALOVIRUS INFECTION.

(E.) Diosi, P. (Timisoara Med. Sch. Inst. Hyg., Rumania) and L. Roth. Path. Microbiol. 33(3):146-152, 1969.

During a 1-yr. study of 8 adults with leukemia, designed to detect viral infections associated with malignant disease, cytomegalovirus was isolated on 2 separate occasions from circulating WBC of a 65-yr.-old woman with chronic lymphatic leukemia. Virus isolation was performed in mixed WBC and fibroblast-type cell culture, and cytopathic changes characteristic of cytomegalovirus were found. The pt. did not have rising titers of complement-fixing antibodies or clinical evidence of cytomegalic inclusion disease. No viremia was detected, and no inclusion bodies were seen in cells sedimented from saliva and urine. The preferential localization and possible long persistence of cytomegalovirus in lymphatic tissues are discussed. An activating role for chemotherapeutic agents cannot be excluded, because virus isolation was preceded by treatment with chlorambucil.

70-1613 INFECTIOUS MONONUCLEOSIS - ALWAYS A PRIMARY INFECTION WITH HERPES-TYPE VIRUS?

(E.) Stevens, D. A. (U. California Los Angeles Med. Ctr.), T. W. Pry and R. A. Manaker. J. Nat. Cancer Inst. 44(3):533-537, 1970.

Sera from 13 pts. (7-25 yr. old) with infectious mononucleosis (IM), obtained at various times before and after the onset of clinical disease, were studied by indirect immunofluorescence for antibodies to the herpes-type virus (Epstein-Barr virus). Most pts. were seronegative before illness and seropositive after onset of disease. Some pre-IM samples were seropositive in low titer, showing a prominent rise in titer after

the onset of disease. The implications of the results with regard to the theory that herpes-type virus causes IM are discussed.

70-1614 SMALL PARTICULATE DEBRIS ADHERING TO CELL SURFACES IN HUMAN LEUKOCYTE CULTURES: RELATIONSHIP WITH PRESENCE OF HERPES-TYPE VIRUS PARTICLES. (E.) Chandra, S. (Chas. Pfizer & Co., Inc. Maywood, N. J.), T. Liszczak and J. H. Monroe. J. Nat. Cancer Inst. 44(3):497-505, 1970.

Non-virus-containing cells with small particulate debris on their cell surfaces were found in human WBC cultures derived from normal subjects and pts. with various tumors (such as Burkitt's lymphoma, reticulum cell sarcoma and acute myelocytic leukemia) and containing herpes-type virus (HTV) particles. The debris sometimes had a few HTV particles and consisted of membranous bodies that varied in shape and size. The percentage of cells with debris was much higher than that of cells infected with HTV. It is concluded that such debris indicates the presence of HTV particles in WBC cultures, and the vesicular bodies constituting the debris contain viral proteins that may produce the membrane immunofluorescence seen in these cultures.

70-1615 EVIDENCE FOR THE PRESENCE OF ANTI-BURKITT TUMOR GLOBULINS IN POOLED HUMAN IMMUNE GLOBULINS. (E.) Young, B. G. (U. Maryland, College Park) and B. E. Swart. Cancer Res. 30(3):763-767, 1970.

Specific immunofluorescence (IF) reactions with EB3 cells, a continuous cell strain derived from Burkitt's lymphoma, were produced by each of 20 commercially-prepared lots of human immune globulins. Titers of IF ranged from 1:80 to 1:640. Growth of EB3 cell cultures was also suppressed by each of the lots. Complement was found to be unnecessary for these reactions. A good correlation was found between growth suppression titers and IF. In 6 human lymphoma and leukemia cell culture lines studied, the suppression of cellular growth was related to the degree of EB virus infection. Globulins responsible for the IF and growth suppression reactions were partially sensitive to 2-mercaptoethanol; they were absorbed by EB3 cells, but not by human amnion cells.

70-1616 ANTIBODIES IN HUMAN SERA TO SOLUBLE AND VIRAL ANTIGENS FOUND IN BURKITT LYMPHOMA AND OTHER LYMPHOBLASTOID CELL LINES. (E.) Vonka, V. (Baylor Coll. Med., Houston, Tex.), M. Benyesh-Melnick and R. M. McCombs. J. Nat. Cancer Inst. 44(4):865-872, 1970.

Comparative indirect immunofluorescence (IF) and complement-fixation (CF) reactivity of human sera were studied with 2 antigens derived from

Burkitt lymphoma cells: a soluble cell extract (S) antigen and a partially purified Epstein-Barr (EB) virus particle (V). Of 177 sera (from normal children and young adults) examined, 128 were positive by the IF test with fixed EB3 cells; 106/128 reacted in the CF test with V antigen, and 72/128 with the S antigen. The 49 sera negative in the IF test were also negative for CF-S and CF-V antibodies. Positive sera revealed a high correlation between IF and CF-V antibody titer, but many CF-S antibody-negative sera had high IF and CF-V antibody titers. It is suggested that the reactivity of sera indicates that the antigens detectable by the IF and CF-V tests are closely related, but that the S antigen is immunologically distinct. No correlation was found between the conc. of S antigen and virus particles or percentage of IF-positive cells in EB virus-containing cells. The S antigen was detected in preparations derived from AMC30 cells (free of detectable EB virions), but was not found in preparations of HeLa, KB or human embryonic lung cells.

70-1617 EFFECT OF METABOLIC INHIBITORS ON MEMBRANE IMMUNOFLUORESCENCE REACTIVITY OF ESTABLISHED BURKITT LYMPHOMA CELL LINES. (E.) Yata, J. (U. Tokyo), G. Klein, J. Hewetson and L. Gergely. Int. J. Cancer 5(3):394-403, 1970.

In 3 lines of cultured Burkitt lymphoma (BL) cells (Maku, Onesmas, Silfere), expression of the Epstein-Barr virus-associated membrane antigen complex was studied after exposure to X-irradiation and metabolic inhibitors. Direct membrane immunofluorescence (MIF) with a BL reference conjugate (F-Mutua) showed a high number of positive cells in the Maku and Onesmas lines when they were cultured in conditions defined as optimal for expression of the membrane antigen. The Silfere line had less than 5% MIF-positive cells. Mitomycin C (7.5-10 µg/ml), methotrexate (15 µg/ml), actinomycin D (0.5-1.0 µg/ml) and X-irradiation (100-200 R) all increased the frequency of positive cells in Onesmas and Maku cultures maintained under conditions which favored a low membrane antigen expression. Puromycin (0.2 µg/ml) decreased the frequency of MIF-positive cells from 50% to less than 10%. Cytosine arabinoside (50 µg/ml) and low temperatures (31° C and 28° C) did not affect MIF in cultures with either high or low membrane antigen expression, but cell growth was suppressed. None of the inhibitors affected the expression of membrane antigens in the Silfere cell line.

70-1618 ETIOLOGIC RELATIONSHIP OF SKIN TUMORS (SKIN LEUKOSIS) OF CHICKENS TO MAREK'S DISEASE. (E.) Sharma, J. M. (Washington Agric. Res. Ctr., Pullman), W. C. Davis and S. G. Kenzy. J. Nat. Cancer Inst. 44(4):901-911, 1970.

A cytopathic effect (CPE) like that of Marek's disease developed in chicken kidney (CK) cell cultures inoc. with homogenates of skin tumors from chickens. Herpes virions were found by electron microscopy in the infected CK cell cultures. The viral CPE was inhibited by 5-iodo-2'-deoxyuridine, and the virus remained strictly cell-associated. Infectivity was destroyed by disruption of infected cells by 3 cycles of quick freeze-thawing. When suspensions of infected CK cells negative for resistance-inducing factor were inoc. into susceptible chicks, a disease picture typical of acute Marek's disease (MD) developed and 3/10 inoc. chicks grew gross skin tumors. The virus was isolated from kidney and skin homogenates of experimentally-infected chickens. It is suggested that the chicken skin tumors studied are related to the MD syndrome.

70-1619 VIRUSES AND THE DEVELOPMENT OF TUMORS. (Rus.) Frolov, A. F. (Kiev Inst. Epidem. Microbiol. Parasitol., USSR). Vrach. Delo (10):5-8, 1968.

In a discussion of experiments with non-inbred albino mice treated with urethan (U), influenza virus (IV) or U and IV combined, the followed data are presented: 70/158, 45/90 and 60/158 mice, resp., survived until the development of the first tumors was observed. Tumors (unspecified) developed in 15/70 (21.4%), 6/45 (13.3%) and 32/60 (53.3%) of these surviving mice, resp. In CC57 mice treated with U alone, IV alone or U combined with IV, survival rates (as above) were 53/108, 45/57 and 33/144 mice, resp., and tumors developed 2/53 (3.7%), 1/45 (2.2%) and 12/33 (36.3%) survivors, resp. The tumors induced by IV, in 2.2% of the CC57 mice, were of the tubular adenoma type (no other details).

70-1620 A NEW TUMOR INDUCING VARIANT OF MOLONEY LEUKEMIA VIRUS. (E.) Abelson, H. T. (NCI, Bethesda, Md.) and L. S. Rabstein. Proc. Amer. Ass. Cancer Res. 10:1, 1969.

70-1621 VIRUS-LIKE PARTICLES IN CULTURED MURINE EPENDYMOBLASTOMA CELLS. (E.) Ames, R. P. (Montefiore Hosp., New York, N. Y.) and R. C. Rubin. Proc. Amer. Ass. Cancer Res. 10:3, 1969.

70-1622 HYPERPLASTIC ALVEOLAR NODULES IN HIGH (+) AND LOW (-) MAMMARY CANCER SUB-LINES OF C3H/Ki MICE. (E.) Bagby, S. P. (Baylor U. Coll. Med., Houston, Tex.), A. G. Liebelt, R. A. Liebelt and K. DeOme. Proc. Amer. Ass. Cancer Res. 10:4, 1969.

70-1623 INFLUENCE OF HORMONES AND MTV ON DNA SYNTHESIS IN NODULE OUTGROWTHS (HAN) OF MOUSE MAMMARY GLAND. (E.) Barnawell, E. B. (U. Nebraska Inst. Cell. Res., Lincoln) and M. R. Banerjee. Proc. Amer. Ass. Cancer Res. 10:4, 1969.

70-1624 REPLICATION OF MOUSE SARCOMA VIRUS MOLONEY STRAIN (MSV-M) IN HUMAN CELLS. (E.) Bioron, M. (St. Louis Hosp. Inst. Leukemia Res., Paris), C. Bernard and J. C. Chuat. Proc. Amer. Ass. Cancer Res. 10:8, 1969.

70-1625 INHIBITION OF POLYOMA REPLICATION IN VITRO BY 6-METHYLMERCAPTOPYRINE RIBOSIDE. (E.) Bowen, J. M. (U. Texas M. D. Anderson Hosp., Houston), R. G. Hughes and L. Dmochowski. Proc. Amer. Ass. Cancer Res. 10:9, 1969.

70-1626 PROTECTION BY ANOTHER MURINE LEUKEMIA VIRUS AGAINST INDUCTION OF FRIEND VIRUS DISEASE. (E.) Buffett, R. F. (Roswell Park Mem. Inst., Buffalo, N. Y.), E. A. Mirand and J. T. Grace, Jr. Proc. Amer. Ass. Cancer Res. 10:11, 1969.

70-1627 CORRELATION OF INFECTIVITY WITH RADIOISOTOPE STUDIES OF THE MAMMARY TUMOR VIRUS (MTV) IN VITRO. (E.) Cardiff, R. D. (U. California Cancer Res. Genet. Lab., Berkeley) and P. B. Blair. Proc. Amer. Ass. Cancer Res. 10:13, 1969.

70-1628 CONCOMITANT LOSS OF VIRIONS AND ANTIGENICITY IN TRANSPLANTED THYMIC LYMPHOMA OF W/FU RATS INDUCED BY RADIATION LEUKEMIA VIRUS. (E.) Carnes, W. H. (U. California, Los Angeles), B. G. Bowman and M. L. Hart. Proc. Amer. Ass. Cancer Res. 10:13, 1969.

70-1629 DECREASED RATE OF SYNTHESIS OF IMMUNOGLOBULIN (IgG) IN RATS INFECTED WITH MOLONEY VIRUS. (E.) Cure, S. F. (California State Dept. Public Health, Berkeley) and N. E. Cremer. Proc. Amer. Ass. Cancer Res. 10:16, 1969.

70-1630 REMISSION OF FRIEND LEUKEMIA IN BDF₁ HYBRID MICE. (E.) Dawson, P. J. (U. Oregon Med. Sch., Portland) and A. H. Fieldsteel. Proc. Amer. Ass. Cancer Res. 10:17, 1969.

70-1631 TRANSPLANTATION IMMUNITY INDUCED BY UV-IRRADIATED SV40 AND DERIVED TUMORS.

(E.) Defendi, V. (Wistar Inst., Philadelphia, Pa.) and F. Jensen. Proc. Amer. Ass. Cancer Res. 10:18, 1969.

70-1632 PRESENCE OF HERPES-TYPE VIRIONS IN CHINESE NASOPHARYNGEAL TUMOR CULTURED IN VITRO. (E.) de-Thé, G. (Int. Ctr. Cancer Res., Lyon, France), J. C. Ambrosioni, H. C. Ho and H. C. Kwan. Proc. Amer. Ass. Cancer Res. 10:19, 1969.

70-1633 STUDIES ON THE NATURE OF SURFACE IMMUNOFLUORESCENCE IN EBV INFECTED CELLS. (E.) Dunkel, V. C. (Roswell Park Mem. Inst., Buffalo, N. Y.), J. S. Horoszewicz and J. T. Grace, Jr. Proc. Amer. Ass. Cancer Res. 10:20, 1969.

70-1634 EFFECT OF FRIEND AND RAUSCHER LEUKEMIA VIRUS UPON δ -AMINOLEVULINIC ACID SYNTHETASE ACTIVITY IN MURINE SPLEEN AND LIVER. (E.) Ebert, P. S. (NCI, Bethesda, Md.) and P. A. Ellsworth. Proc. Amer. Ass. Cancer Res. 10:21, 1969.

70-1635 TREATMENT OF PRIMARY MOLONEY SARCOMA VIRUS (MSV)-INDUCED TUMORS IN BALB/c MICE. (E.) Fefer, A. (U. Washington Sch. Med., Seattle) and M. Gaston. Proc. Amer. Ass. Cancer Res. 10:23, 1969.

70-1636 RELATIONSHIPS BETWEEN TUMOR SPECIFIC ANTIGENS AND VIRUS PARTICLES IN RAT LYMPHOMAS INDUCED BY RADIATION LEUKEMIA VIRUS. (E.) Ferrer, J. F. (Stanford U. Med. Sch., Calif.) and F. Gibbs. Proc. Amer. Ass. Cancer Res. 10:24, 1969.

70-1637 BIOPHYSICAL STUDIES OF NUCLEI FROM NORMAL AND FRIEND LEUKEMIA VIRUS (FLV) INFECTED MOUSE SPLEEN. (E.) Fiel, R. J. (Roswell Park Mem. Inst. Springville Labs., N. Y.) and J. L. Ambrus. Proc. Amer. Ass. Cancer Res. 10:24, 1969.

70-1638 ISOLATION AND IDENTIFICATION OF A HELPER VIRUS FOUND IN THE MOLONEY SARCOMA-LEUKEMIA VIRUS COMPLEX. (E.) Fischinger, P. J. (NCI, Bethesda, Md.). Proc. Amer. Ass. Cancer Res. 10:25, 1969.

70-1639 EFFECTS OF CULTURE CONDITIONS ON SV40 TRANSFORMED HUMAN AMNION CELLS. (E.) Fogh, J. (Sloan-Kettering Inst., New York, N. Y.) and E. V. Gaffney. Proc. Amer. Ass. Cancer Res. 10:26, 1969.

70-1640 STUDIES ON THE ERYTHROPOIETIC ACTIVITY OF MURINE VIRUS-INDUCED LEUKEMIC CELLS CLONED IN VITRO. (E.) Friend, C. (Mt. Sinai Sch. Med., New York, N. Y.) and W. Scher and G. B. Rossi. Proc. Amer. Ass. Cancer Res. 10:27, 1969.

70-1641 SV40 TRANSPLANTATION ANTIGEN (TrAg) DURING PRIMARY INFECTION OF AFRICAN GREEN MONKEY KIDNEY CELLS. (E.) Girardi, A. J. (Wistar Inst., Philadelphia, Pa.) and V. Defendi. Proc. Amer. Ass. Cancer Res. 10:29, 1969.

70-1642 THE INCIDENCE OF MAMMARY TUMORS IN X/Gf MICE FOSTER-NURSED BY IBA/Gf FEMALES. (E.) Goldfeder, A. (New York U. Cancer Radiobiol. Res. Labs., N. Y.) and A. K. Ghosh. Proc. Amer. Ass. Cancer Res. 10:31, 1969.

70-1643 INDUCTION OF INFECTIOUS MONONUCLEOSIS IN MAN BY THE HERPES-TYPE VIRUS (HTV) IN BURKITT LYMPHOMA CELLS IN TISSUE CULTURE. (E.) Grace, J. T., Jr. (Roswell Park Mem. Inst., Buffalo, N. Y.), J. Blakeslee, Jr. and R. Jones, Jr. Proc. Amer. Ass. Cancer Res. 10:31, 1969.

70-1644 VIRUS PARTICLES IN GUINEA PIG LEUKEMIA AND IN CAT MAMMARY CARCINOMA. (E.) Gross, L. (VA Hosp., Bronx, N. Y.) and D. G. Feldman. Proc. Amer. Ass. Cancer Res. 10:33, 1969.

70-1645 EXPERIMENTAL STUDIES WITH CELL-FREE EXTRACTS FROM HUMAN OVARIAN TUMORS. (E.) Hartmann, P. Proc. Amer. Ass. Cancer Res. 10:36, 1969.

70-1646 REGENERATION AND LYMPHOMAGENESIS IN THYMUS RETICULAR CELL GRAFTS IN THE PRESENCE OF GROSS VIRUS. (E.) Hays, E. F. (U. California Sch. Med., Los Angeles). Proc. Amer. Ass. Cancer Res. 10:37, 1969.

See also abstract nos.: 1442,1443,1459,1552,1675

- 70-1647 GEOGRAPHIC PATTERNS OF U. S. CANCER MORTALITY. (E.) Krasnow, S. Scientia (Milano) 104(11-12):592-601, 1969.

A map showing the geographical distribution by county for all types of malignant neoplasms (combined) in the U. S. (excluding Alaska and Hawaii), for 1951 and 1961 is presented, using crude death rates/100,000 population for all races and both sexes. The pattern of distribution did not appear to correspond with any of a number of socioeconomic, meteorological or geological patterns. A correspondence of geographical distribution with patterns for annual rainfall, soil type, and geographical patterns of occurrence of certain forms of plants and of soil microorganisms or viruses was seen. Hypotheses are advanced implicating certain types of soil microorganisms as possible etiological factors in the relationship between malignancy rates and soil moisture.

- 70-1648 GEOGRAPHIC AND SECULAR VARIATION IN MORTALITY FROM MALIGNANT DISEASE IN OKLAHOMA 1956-1965. (E.) Assal, N. R. (U. Oklahoma Sch. Health, Oklahoma City) and R. D. Lindeman. J. Okla. Med. Ass. 63(1):17-28, 1970.

Mortality from cancer of the g.i. tract in Oklahoma during 1956-1965 was analyzed; age- sex- and race-specific and adjusted death rates were tabulated for 1956-1960 and 1961-1965 and analyzed in relation to environmental factors. Secular trends were consistent with those reported for the rest of the U. S.; the major trend noted was a significant decrease in mortality from stomach cancer among whites. Geographical distribution of adjusted mortality rates showed that cancer of the g.i. tract was more prevalent in northwestern counties of the state, a rural area at high elevation underlain by salt and inhabited by people of upper socioeconomic status. Distribution of g.i. tract malignancies in relation to race and sex are also discussed.

- 70-1649 A PROPOS OF SUMMARIZING INDICES FOR COMPARISON OF CANCER INCIDENCE DATA. (E.) Staszewski, J. (Inst. Oncol., Gliwice, Poland) Neoplasma (Bratisl.) 16(3):321-323, 1969.

Methods of expressing age-standardized rates (a summary of a set of age-specific rates) were presented in an attempt to minimize the distortion due to the lower quality of cancer diagnosis in the aged. The "truncated age-standardized rate," proposed by Dale and Cook, is compared to the "age-adjusted index," which sums up the normal age-standardized rate in 2 ranges, 0.-64 yr. and 65 yr. and older. It is considered that the latter method yields indices which are more valid and more readily comparable to "total" age-adjusted rates.

- 70-1650 CANCER IN THE GAUTIER HOSPITAL. A PRELIMINARY STUDY. (Sp.) Kourie F., M. and G. Lora V. Rev. Dominic. Der. 2(2): 128-135, 1968.

Of 10,000 biopsies and 558 autopsies performed in a workers' hospital in the Dominican Republic, 67.6% and 95.5%, resp., were performed on male pts. Cancer was confirmed in 11.49% and 16.1% of the cases, resp. Frequency of cancer by age groups increased steadily up to 59 yr., then decreased progressively, with 45% of the cases found between 40-59 yr. of age. Biopsy confirmation of cancer in men was found most often in the skin (16.6%), lymphatic tissues (15.5%), penis (8.5%), stomach (5.9%), liver (5.7%), colon (5.7%), prostate (5.0%), bone (4.1%), buccal cavity (3.8%) and lung (3.0%). In women, it was found in the uterine cervix (35.9%), breast (15.6%), skin (6.2%), colon (4.3%), stomach (3.2%), liver (3.2%), uterine corpus (2.9%), thyroid (2.4%), ovary (2.1%) and bladder (2.1%). In autopsied men, cancer was confirmed most often in the liver (32.5%), lung (15.1%), stomach (11.6%), lymphatic tissues (8.1%), pancreas (4.6%) and prostate (4.6%). The need for prophylactic circumcision in the male and routine cytologic study of the cervix in the female is emphasized.

- 70-1651 THE EPIDEMIOLOGY OF CARCINOMA. (II). A STUDY EMPLOYING ISRAELI STATISTICAL MATERIAL. (Ger.) Kallner, G. Med. Welt 20(18): 1069-1079, 1969.

The percentage distribution is presented for all Israeli cancer cases at the time of the study, by national origin of the pts., subdivided into high, medium and low incidence groups. Tabulated for cancers at 17 primary sites are the absolute number of pts. who had died or were hospitalized at the time of the study; the percentage of all cancers represented by that particular site in other countries, among Israelis of North African and Middle Eastern ("oriental") extraction, and among Israelis of European and American ("occidental") extraction; the male:female ratio (similarly subdivided); the mortality rate/100,000 population (similarly subdivided); the ratio of "occidental" to "oriental" Israeli mortalities; the percentage distribution of cases among 6 age groups (0-24 yrs., then by decades to 65 yr. and older); the percentage distribution of cases by national origins of the pts.; the relationship of 1950-1954 to 1958-1961 mortality rates for "oriental" and "occidental" Israelis; and the percentage probability of fatal outcome. Clear-cut differences between groups of different national origins are demonstrated in many instances.

70-1652 EPIDEMIOLOGIC STUDY OF MALIGNANT TUMORS IN HAMBURG 1960-1962. (Ger.) Maass, H. (Univ. Hosp. Eppendorf, Hamburg, Germany), H. Sachs and B. Pauka. Z. Krebsforsch. 73(1):1-45, 1969.

In a detailed statistical study of cancer mortality in 42 districts of Hamburg (1960-1962), the cancer mortality rates/10,000 women were given as follows: for all sites combined, 74.0; breast, 12.3; cervix, 7.9; uterus, 3.5; ovary, 6.7; stomach, 10.0; liver and biliary tract, 5.0; and respiratory tract, 3.7. The cancer mortality rates/10,000 men were: combined, 90.9; stomach, 17.1; colon, 4.7; rectum, 4.3; and respiratory tract, 24.7. Standardized age-adjusted data showed significant differences in cancer mortality in different districts of the city. Among women, the most pronounced regional differences were found for cancer of the cervix and uterus, ovary and Fallopian tubes, stomach, liver and bile ducts, and all tumors combined; in men the largest differences were seen for all cancers combined and for cancer of the respiratory tract and colon. Among women, a significant positive correlation was noted between industrial density and mortality from cervix and uterus cancer, as well as the total cancer mortality rate. A similar relationship was seen between industrial density and the regionally different rates in working women (industry or trades) for cancer of the breast and cervix and for all cancers combined. A negative correlation was noted between fertility and carcinomas of the ovary and Fallopian tubes. Among men, a positive correlation was seen between population density and cancer of the colon, and between industrial density and cancer of the respiratory tract and colon. Analysis of 2000 male deaths from cancer of the respiratory tract revealed a high risk for lung cancer among bricklayers, carpenters, painters, sheet metal workers, locksmiths, dock workers, land and water transportation workers and office workers.

70-1653 CARCINOMA OF THE LUNG IN ICELAND. A SUMMARY AND SOME REFLECTIONS CONCERNING MORE RECENT PRINCIPLES FOR DIAGNOSIS AND TREATMENT. (E.) Thorarinsson, H. (Univ. Hosp. Reykjavik, Iceland). Scand. J. Thorac. Cardiovasc. Surg. (1):31-38, 1969.

The av. annual incidence of lung cancer in Iceland during the period 1955-1964 was 12.1/100,000 for men and 6.5/100,000 for women; during 1955-1959, the rate for men was 10.3 and for women, 5.1, while for the period 1960-1964, it was 13.6 for men and 7.8 for women. From 1931-1964, a major increase was seen among women, especially in urban areas, with a definite correlation with an increased sale of cigarettes. Among secondary school pupils in Reykjavik in 1959, the number of smokers increased directly with age from 34.8% among boys aged 13-17 yr.; among girls, the percentage who smoked ranged between 16.4% and 19.9%. The increase in lung cancer in Iceland

was well correlated with the increased consumption of tobacco.

70-1654 LUNG CANCER IN THE HUNGARIAN PLAIN. (E.) Ormos, J. (Univ. Med. Sch., Szeged, Hungary), G. Karácsonyi, F. Biliczki and F. Szönyi. Neoplasma (Bratisl.) 16(6):667-675, 1969.

A study of 10,124 autopsies performed in Szeged, Hungary between October 22, 1921 and June 30, 1959, showed primary lung cancer in 196/5438 males and 43/4686 females, mostly in the sixth decade. The av. age of autopsied pts. increased from 44 in 1921-24 to 61 in 1955-1959; the proportion of lung cancer increased from 0.43% to 3.69% (males, 0.84-6.11%; females, 0-1.06%). The frequency of all cancers increased from 8.39-19.5%. Anaplastic small cell carcinoma was the most frequent histological type (28.4%), followed by epidermoid carcinoma (25.9%), anaplastic large cell carcinoma (10.8%), adenocarcinoma (10.8%) and alveolar carcinoma (3.8%). The increased incidence of lung cancer in males, but not females, correlated highly with increased smoking (except for adenocarcinoma). The ratio of cancer cases among heavy smokers compared to nonsmokers was 13:1, for medium smokers, 8:1, and for light smokers, 11:1.

70-1655 THE CAUSES OF DEATH OF SOUTH AFRICAN DOCTORS AND DENTISTS. (E.) Dean, G. (65 Merrion Square, Dublin). S. Afr. Med. J. 43(17):495-500, 1969.

A census performed in 1964 showed 7779 doctors (6949 males, 833 females; 7293 White, 317 Asian, 73 Coloured and 106 Bantu) and 1201 dentists (1186 males, 15 females; 1191 White and 10 Asian) residing in South Africa. From 1960-1966 (inclusive), 489/7779 doctors (462 White, 10 Asian, 3 Coloured, 14 Bantu) and 92/1201 dentists (all White) died of various diseases, including 60/489 (9 females) and 15/92, resp., from cancer. Although mortality rates for doctors and dentists were lower than expected for the general population, frequency of death due to lung cancer was markedly high. There were 22 deaths due to lung cancer among doctors (17 males, 5 females), while the expected values were 19 and 0.5, resp., indicating the markedly high lung cancer death rate in women doctors. Review of smoking habits showed 15/17 males as cigarette smokers (11/15 smoked more than 30/day), 1 heavy cigar smoker and 1 nonsmoker; 4/5 female doctors who died of lung cancer were heavy cigarette smokers (all more than 30/day). Lung cancer was the most common cause of death in dentists. Other significant deaths included lymphosarcoma (6 as compared to an expected number of 1) and leukemia in male doctors (6 as compared to 3 expected). Of the nonwhites, the death rate among Bantu doctors was significantly high (14 as compared to 3 expected); 1/14 was due to cancer of the pancreas. It is concluded that the relatively

high death rate from lung cancer is related to the number of cigarettes smoked.

70-1656 UPPER ALIMENTARY TRACT CANCER IN NATAL INDIANS WITH SPECIAL REFERENCE TO THE BETEL-CHEWING HABIT. (E.) Schonland, M. (U. Natal Durban Med. Sch.) and E. Bradshaw. Brit. J. Cancer 23(4):670-682, 1969.

A 1964 survey of g.i. cancer in Hindus and Moslems in Durban, Natal indicated a higher incidence of cancer of the upper g.i. tract (tongue, buccal cavity, pharynx, esophagus and stomach) at all sites in females. Analysis of social habits showed a significant difference in the habit of chewing betel nut between Indian males (8.3%) and females (54.2%) aged 20 or over; the proportion who chewed betel increased with age. The mean age at which betel chewing began was 20-24 yr.; more females than males were heavy chewers (more than 4 times/day). No significant difference was found between Hindus and Moslems; the more westernized persons (males and younger persons) indulged less in this habit. The major components of the betel quid in this population are betel nut, its leaf and lime; tobacco is added infrequently.

70-1657 AIR POLLUTION AND ITS HEALTH ASPECT IN TOKYO AREAS. (E.) Toyama, T. (Keio U. Sch. Med., Japan). Asian Med. J. 11(12):5-15, 1968.

The various aspects of air pollution, including contamination from SO₂, suspended particulate matter, and automobile fuel consumption, as they pertain to public health in Tokyo, Japan are presented. Reference is made to studies of respiratory symptoms and pulmonary function. The death rate in urban areas of metropolitan Tokyo was higher than in surrounding areas. Study of age-adjusted death rates for lung and stomach cancer indicated an increase in incidence of lung cancer, whereas the stomach cancer death rate remained unchanged. The association of increased smoking in Japan and increased lung cancer frequency is also discussed.

70-1658 NASAL CANCER IN THE NORTHAMPTONSHIRE BOOT AND SHOE INDUSTRY. (E.) Acheson, E. D. (Oxford Record Linkage Study, England), R. H. Cowdell and B. Jolles. Brit. Med. J. 1(5693):385-393, 1970.

A survey of the incidence of nasal cancer in Northamptonshire for the 15-yr. period 1953-1967 showed that 21/46 pts. (19 males, 2 females) had at some time been employed in the boot and shoe industry. Five similar cases, diagnosed either before 1953 or after 1967, were obtained from other sources. The incidence of nasal cancer was significantly higher for male boot and shoe workers than for males of all occupational classes selected for comparison. About 85% of the

classifiable cases occurred in the relatively small number of workers (about 20% of the skilled workers) exposed to the dusts of materials used in footwear manufacture, especially leather, fiberboard, cork and rubber. No such cases were found among persons exposed to the sprays and lacquers used in finishing shoes. It is suggested that 2 possible carcinogenic factors are present; one related to the induction of nasal adenocarcinoma, the other to squamous cell and possibly other types of carcinoma of the nasal cavity and sinuses. The estimated mean latent period for the adenocarcinomas (54.6 yr.) was significantly longer than for the squamous cell, transitional cell and anaplastic tumors (41.7 yr.). A probable increased risk of nasal adenocarcinoma in the footwear repairing industry was suggested. The possible contributory role of snuff-taking in both industrial and non-industrial nasal cancer is discussed. Some of the persons with nasal cancers who had worked at occupations other than shoe manufacturing or repair, had been exposed occupationally to other types of dust, especially flour (bakery workers).

70-1659 A STUDY OF LUNG CANCER AND BRONCHITIS MORTALITY IN RELATION TO COAL-MINING IN SCOTLAND. (E.) Crofton, E. C. (U. Edinburgh). Brit. J. Prev. Soc. Med. 23(3):141-144, 1969.

Deaths from lung cancer in coal mining areas of Scotland obtained from the Annual Reports of the Registrar-General for 1958-1963 were compared with the expected numbers of deaths in these areas, allowing for differences in age structure of the population and the relative degree of urbanization. Results showed a significant excess of bronchitis and lung cancer in males in areas concerned with coal mining by comparison to non-mining areas. Among females in the coal-mining areas, there were more deaths from bronchitis, but fewer deaths from lung cancer. Hospital discharge rates (not adjusted for age) for lung cancer and bronchitis showed similar trends. Scottish miners smoked an av. of 106.5 cigarettes/week, compared to 141/week for the overall male population of Scotland.

70-1660 ENVIRONMENTAL FACTORS IN THE AETIOLOGY OF LUNG CANCER AND BRONCHITIS. (E.) Ashley, D. J. B. (Morriston Hosp., Swansea, Wales). Brit. J. Prev. Soc. Med. 23(4):258-262, 1969.

A multiple regression analysis of the relationship between mortality from lung cancer and bronchitis, and a series of environmental factors, was performed on data from 53 county boroughs of Wales and England for the period 1958-1963. A significant positive association with increasing population density and lower social class in lung cancer in men and women was observed; a significant negative association was found between SO₂ conc. in the atmosphere and mortality from lung cancer in men. A negative association was

also seen between the conc. of the coal and textile industries, and mortality in all groups; this association was significant in men with lung cancer. It is suggested that the effect of the textile and coal industries in reducing lung cancer mortality could be related to an enhanced state of immunological preparedness in the lungs of persons constantly exposed to dust. A similar mechanism may prevail for SO_2 , or there may be a more specific effect on the reaction between S-containing amino acids in the bronchial mucosa and carcinogenic agents in the air.

70-1661 ENVIRONMENTAL FACTORS IN THE AETIOLOGY OF GASTRIC CANCER. (E.) Ashley, D. J. B. (Morriston Hosp., Swansea, Wales). Brit. J. Prev. Soc. Med. 23(3):187-189, 1969.

The relationship between mortality from stomach cancer in both sexes and several environmental variables (population density, social status, smoke and SO_2) for 53 towns of England and Wales, was analyzed by the method of multiple regression. Standardized mortality ratios were calculated for 1958-1963. A positive association was seen between stomach cancer and the general social factors, population density and social class; a positive association with air pollution (SO_2 and smoke) was seen for men, but not for women. A positive association between stomach cancer and the presence of dusty industries (coal mining and textile manufacturing) was also found. It is suggested that the mechanism of the association with the last 2 environmental factors may be related to inhalation of carcinogenic substances, followed by swallowing of sputum. An alternative suggestion was that food may be contaminated before ingestion by carcinogens in the atmosphere or in dust.

70-1662 THE GEOGRAPHICAL COMPARISON OF MORTALITY FROM CANCER OF THE STOMACH AND ULCER OF THE STOMACH IN JAPAN. (E.) Hirohata, T. (Kyushu U., Fukuoka City, Japan) and M. Kuratsune. Brit. J. Cancer 23(3):465-479, 1969.

Mortality rates for cancer of the stomach were correlated with mortality from stomach ulcers in the 46 prefectures of Japan during 1949-1951 and 1959-1961, inclusive. Av. annual mortality rates/100,000 population for stomach cancer in all of Japan were 46.28 in males and 28.13 in females in 1949-1951, increasing to 50.40 and 30.62, resp., in 1959-1961. Corresponding stomach ulcer mortality rates were 30.64 in males and 11.80 in females in 1949-1951, decreasing to 13.25 and 5.79, resp., in 1959-1961. No geographical correlation was observed between the 2 diseases, based on distribution in the same sex in the same period of yr.; no correlation was noted between mortality from stomach ulcers in 1949-1951 and stomach cancer in 1959-1961. This does not support the hypothesis of a close causative relation between the 2 diseases. A highly positive

geographical correlation of stomach cancer was found between males and females and between 1949-51 and 1959-61. This was also true for stomach ulcers, but to a lesser degree. High stomach ulcer mortality rates (120% or more of the rates for all of Japan) were clustered in East-Kanto and the Kyushu Districts, while the Hokkaido, Aomori, Tokyo and Aichi prefectures and Shikoku District showed low rates (less than 80% of the national rate). High stomach cancer mortality rates were seen in areas of the northeastern part of Honshu that borders the Sea of Japan; low-rate areas were concentrated in the Kyushu (including Nagasaki) and Shikoku Districts. Nara prefecture showed a high rate; Shizuoka and Iwate prefectures had low rates.

60-1663 RESIDENCE, AGE, RACE AND RELATED FACTORS IN THE SURVIVAL AND ASSOCIATIONS WITH SALIVARY TUMORS. (E.) Keller, A. Z. (DM&S Res. Serv. Geographic Epidem., Washington, D. C.). Amer. J. Epidem. 90(4):269-277, 1969.

A nationwide VA hospital study (1958-1962) of salivary gland tumors (of the mouth and associated structures) in 90 pts. with malignant tumors, 90 age-matched controls and 59 pts. with benign tumors, showed no associations with heavy smoking or drinking, residence, race, syphilis, diabetes mellitus, rheumatoid arthritis, extra-oral neoplasms and cirrhosis of the liver; the over-all risk of malignant tumors increased with age.

70-1664 MULTIPLE PRIMARY MALIGNANT TUMOURS. AN AUTOPSY STUDY OF A CIRCUMSCRIBED POPULATION. (E.) Berge, T. (U. Lund Gen. Hosp., Malmö, Sweden), L. Cederqvist and J. Schönebeck. Acta Path. Microbiol. Scand. 76(2):171-183, 1969.

A study of the frequency of multiple tumors in a defined population (Malmö, Sweden; 250,000 inhabitants) revealed 5523 tumors in 4895/11,098 (44.1%) persons autopsied during the 9-yr. period 1958-1966. Multiple tumors were found in 572 (11.7%); of these, there were 521 (10.6%) with 2, 46 (0.9%) with 3 and 5 (0.1%) with 4 tumors. The types and locations of multiple malignant tumors were about the same as for solitary tumors. At autopsy, the frequency of multiple tumors increased with the survival time after treatment of the first tumor.

70-1665 INCIDENCE OF MULTIPLE PRIMARY CANCERS. III. CANCERS OF THE RESPIRATORY AND UPPER DIGESTIVE SYSTEM AS MULTIPLE PRIMARY CANCERS. (E.) Berg, J. W. (NCI, Bethesda, Md.), D. Schottenfeld and F. Ritter. J. Nat. Cancer Inst. 44(2):263-274, 1970.

Of 9415 pts. with squamous cell carcinomas of the respiratory or upper digestive tract or other lung cancers, observed at Memorial Hospital (New York City) for a total of 23,802 pt.-yr. of

observation, 518/9415 developed second primary cancers at other sites (150-250% of the expected incidence). When the site of the initial lesion was the lip, the observed/expected (O/E) ratio for a second cancer was 1.6:1; in pts. with index cancers of the oral cavity and pharynx, esophagus, larynx and lung, the O/E ratios were 1.9:1, 2.5:1, 2.1:1 and 1.8:1, resp. Pts. with index tumors of the nasal cavity, paranasal sinuses and nasopharynx did not have an increased incidence of a second cancer. The other cancers were localized primarily in the respiratory and upper g.i. tracts (73%) and skin (20%); tumors of other sites comprised the remaining 7%. Pts. with index cancers of the lip showed a high risk of skin and intraoral cancers. Risks of cancer of the esophagus were higher in pts. with index cancers of the tongue, palate or pharynx than in pts. with other types of intraoral cancer.

70-1666 THE ASSOCIATION BETWEEN CARCINOMA OF THE PANCREAS AND DIABETES MELLITUS. (E.) Karmody, A. J. (Roy. Infirm., Aberdeen, Scotland) and J. Kyle. Brit. J. Surg. 56(5): 362-364, 1969.

Pts. with histologically confirmed carcinoma of the pancreas in northeastern Scotland during the 13-yr.-period 1955-1967 were studied for disturbance in carbohydrate metabolism. The incidence rate was 4.64/100,000/yr., with 265 pts. (128 men, 137 women) studied. Diabetes was found in 51/265 cases, according to the criteria of the study. The age distribution of cases with and without diabetes were similar. Of the 51 pts., the majority were considered unstable, and in 45 the interval between diagnosis of the two diseases was less than 2 yr. It is suggested that unstable hyperglycemia and glycosuria in pts. over 60 yr. of age may be a warning sign of carcinoma of the pancreas, rather than the result of it.

70-1667 SUPERFICIAL CANCER IN NIGERIA. (E.) Oluwasanmi, J. O. (Univ. Coll. Hosp., Ibadan, Nigeria), A. O. Williams and A. F. Alli. Brit. J. Cancer 23(4):714-728, 1969.

A study of superficial cancers (excluding lip and metastatic tumors, and benign neoplasms) in 435 Nigerians during the period 1960-1967 showed that 67% had squamous cell carcinoma, 4.8%, basal cell carcinoma, 24.3%, malignant melanoma, and 3.4%, Kaposi's sarcoma. Among 292 with squamous cell carcinoma, there were 62 women with tumors of perineal skin and anal canal; ages ranged from 18-75, with an av. of 52 yr. for males and 45 for females. The role of phagedenic ulceration, trauma and infection as etiological factors was discussed. Malignant melanoma was seen in 106 pts. (57 males, 49 females), with an av. age of 50 for both sexes. Basal cell carcinoma was observed in 12 men and 9 women, with an av. age of 47 and 35 yr., resp., while 15 pts., all males, had Kaposi's sarcoma (av. age, 43 yr.). Of the

435 pts., 15 (3.4%) were complete albinos (3 female and 12 males); 8 males had squamous carcinoma, 3 had basal cell carcinoma and 1 had sebaceous gland carcinoma. Of the 3 women, 1 each had squamous carcinoma, basal cell carcinoma of the skin and malignant melanoma of the anal canal. None of the albinos had cutaneous melanoma. It is suggested that variations in relative frequencies of the various superficial cancers in different races can be attributed to different environmental factors conditioned by the degree of skin pigmentation.

70-1668 DISTRIBUTION OF MALIGNANT TUMORS OF THE LIP IN CALABRIA BETWEEN 1963 AND 1968. (It.) Grande, P. (Ctr. Diagnosis Care Tumors, Catanzaro, Italy). Rass. Int. Clin. Ter. 49(24):1554-1558, 1969.

In Italy, the proportion of deaths due to cancer of the lip, as compared to all cancer deaths, decreased progressively between 1953-1965, from 3.83 to 2.20/1000. The male:female ratio was essentially constant at 8:1. The frequency/1000 cancer deaths in Catanzaro and Cosenza Provinces in 1963 was 3.61 and 7.92, resp.; in 1964, 1.64 and 3.83, resp.; and in 1965, 3.06 and 10.88, resp. The absolute number of deaths during this 3-yr. period was 5 and 12, resp. During the same interval, there were no deaths due to cancer of the lip in Reggio Calabria. The absolute number of non-fatal cases/yr. seen in Catanzaro Province between 1963-1968, inclusive, was 7, 5, 7, 1, 3 and 5, resp., with a male:female ratio of 22:6. During the same period, 1 case was seen in Cosenza Province in 1965, 4 in 1967 and 6 in 1968; all were women. One case, also a woman, was seen in Reggio Calabria in 1967. The youngest pt. was a 7-yr.-old girl; the oldest, an 82-yr.-old woman. In 38/40 cases (total), only the lower lip was involved; in 1/40, only the upper lip. An additional 37 pts. were treated by the Catanzaro Tumor Center during this same period, consisting of 28 men and 9 women. Only the lower lip was involved in 35/37; only the upper lip, in 2/37. Survivals among 5/37 who were followed ranged from 2-11 yr., at the time of report. In all groups reported, the greatest number of cases were in the 51-60 and 61-70 yr. age groups.

70-1669 FAMILIAL ESOPHAGEAL CARCINOMA. (Sp.) Freytes, M. A. (Rivera Indarte 77, Cordoba, Argentina) and J. Carri. Rev. Fac. Cienc. Med. Cordoba 26(2):215-218, 1968.

A 57-yr.-old woman presented with a fatal, anaplastic carcinoma of the esophagus, confirmed by biopsy of a supraclavicular lymph node. At age 59, one brother presented with a fatal, poorly differentiated carcinoma of the esophagus, confirmed by biopsy and at the time of gastrostomy; at age 65, a second brother presented with an epidermoid carcinoma of the same site, also confirmed by biopsy and at the time of surgery.

That the mother of the 3 pts. had died of an unspecified cancer of the intestine and a third brother had died of an unspecified cancer of the stomach.

70-1670 BLOOD GROUPS AND CANCER OF THE LARYNX. (Ger.) Bruchmüller, W. (Univ. Ear Nose Throat Clin., Halle/Saale, Germany) and G. Eggemann. Z. Laryng. Rhinol. Otol. 47(12):958-962, 1968.

Blood group and Rh factors were determined for 152 pts. with confirmed cancers of the larynx and for 137,906 healthy blood donors. Both groups were drawn from 4 university hospitals in East Germany. No significant differences were found among the pts. as compared to the healthy subjects and to the normal distribution of blood groups; nor were there any significant differences with respect to the Rh factor.

70-1671 BURKITT TUMOR AND ALLIED DISORDERS IN JAPAN. (E.) Sugano, H. (Cancer Inst., Hiroshima-ku, Tokyo). Gann Monogr. 7:35-47, 1969.

Report of a histological study of lymphoma among Japanese, emphasizing lymphoma in children, lymphoma in Okinawa and lymphoma of the nasopharynx. In 1966, the incidence of lymphoma in Japan was 1.91/100,000 population in adult males and 1.66 in adult females. Of 91 biopsy cases (excluding children and cases from Okinawa area) 61.1% were reticulum cell sarcoma, 34.4% lymphosarcoma and 4.5% Hodgkin's disease; 2/7 with a "starry-sky pattern" resembled Burkitt's lymphoma (BL). Among 569 autopsy cases in 1959-1966, 201 (7.8%) were in children under 15 yr. of age. Of 22 biopsy cases in children, 7 (30%) were reticulum cell sarcoma and 11 (48%) were lymphoblastic lymphoma; 1/4 cases of poorly differentiated lymphocytic lymphoma resembled BL. The incidence of lymphoma in Okinawa was almost double that in Honshu, Japan; in 1966, it was 3.35/100,000 population in males and 3.49 in females. Such great variation is attributed to geographic and climatic differences of the 2 areas. Over a 5-yr. period in Okinawa, no classical BL involving the jaw was found, but 5 lymphoblastic lymphomas with a "starry-sky" pattern histologically resembling BL were found. No lymphomas resembling BL were found among 110 lymphomas of the upper respiratory tract during 1959-1967.

70-1672 LEUKEMIA IN ATOMIC BOMB SURVIVORS. HIROSHIMA, 1946-1967. (Jap.) Hirose, T. (Hiroshima U., Res. Inst. Nuclear Med. Biol., Japan) Acta Haemat. (Jap.) 31(5):765-771, 1968.

Statistical studies on leukemia that developed from 1946-1967 in persons exposed to the atomic bomb (within 5,000 meters from the hypocenter) in Hiroshima revealed 168 cases of leukemia, including 68 of the chronic myeloid type. The

incidence rate was 8.34/100,000/yr. for 1951-1959; it then decreased. The death rate from leukemia in survivors was 7.63/100,000/yr., compared to 2.14 in non-exposed persons and 2.32 for all of Japan. The incidence of leukemia was markedly high in persons exposed within 2,000 meters. Based on 1960 census data, the incidence in survivors exposed at a distance of 3,000-5,000 meters was 4.04. The ratio of chronic to acute type decreased with increase in distance from the hypocenter, but from 3,000-5,000 meters the ratio was higher than that for all Japan. Since 1950 there were 63 cases of leukemia among persons who entered Hiroshima City soon after the atomic bomb explosion. The incidence of 45 cases among persons who entered within 3 days after the explosion was high, 9.69; 24 of the cases were of the chronic myeloid type.

70-1673 CHILDHOOD LEUKEMIA MORTALITY IN JAPAN 1947-1966: WITH SPECIAL REFERENCE TO THE GROUP OF UNDER FIVE YEARS OF AGE. (E.) Nishiyama, H. (Aichi Cancer Ctr. Res. Inst., Nagoya, Japan). Gann 60(5):569-581, 1969.

A survey of childhood leukemia in Japan during 1947-1966 revealed increasing mortality rates, particularly among females in the 5-14 yr. age group. There was a decrease in mortality rates for those under 3 yr. of age, but a continual increase between 3 and 4 yr. of age. The peak rate was noted in the 3-yr. age group since 1957, and decline in rate was first observed in those under 1 yr., following a peak in 1960. Mean survival time ranged from 0.67-0.87 yr.; survival increased with advancing age of onset up to age 2 yr. The decline of mortality rate in children less than 3 yr. of age was attributed to the combined effect of a decline in incidence and prolongation of survival time. The peak of mortality rate at 3 yr. was largely due to the high incidence of leukemia at this age, and probably also due to the prolongation of survival time.

70-1674 RELATIVE FREQUENCY AND MORTALITY RATE OF VARIOUS TYPES OF LEUKEMIA IN JAPAN (ADDENDUM). (E.) Nishiyama, H. (Aichi Cancer Ctr. Res. Inst., Nagoya, Japan) Gann 60(3):343-346, 1969.

The annual mortality rates/million population for 9 types of leukemia in Japan from 1965-1966 and 1959-1966, tabulated in 5-yr. age groups, are presented. The mortality rates showed an increase through all age groups in both sexes, which was especially marked in those over 60 yr. of age. Mortality rates increased to a lesser degree in younger age groups.

70-1675 AN EPIDEMIOLOGICAL STUDY OF LEUKEMIA IN JAPAN, WITH SPECIAL REFERENCE TO THE PROBLEM OF TIME-SPACE CLUSTERING. (E.)

Hirayama, T. (Nat. Cancer Ctr. Res. Inst., Chuo-ku, Tokyo). Gann Monogr. 7:5-19, 1969.

In Tokyo and surrounding areas, the annual trend of leukemia in the 2-4-yr. age group showed striking fluctuation similar to that of the measles. A useful theoretical model for the age incidence patterns of childhood leukemia was made by separating age incidence into 2 groups, 0-1 yr. and 2-4 yr. Significant clustering was found within 1-yr., but not 2-yr., intervals and the distance between temporal pairs was significantly less in 2 districts. As an isolated example of time-space clustering, 5 cases of acute leukemia found within 2 yr. among 2-6-yr.-old children in a limited area of a town of 23,657 in Japan are presented.

70-1676 STUDIES ON EPIDEMIOLOGY OF LEUKEMIA IN TOKAI DISTRICT IN JAPAN - STATISTICAL APPROACHES TO LEUKEMIA CLUSTERS. (E.) Yamada, K. (Nagoya U. Sch. Med., Japan), K. Ota and J. Mokuno. Acta Haemat. (Jap.) 31(5):756-764, 1968.

The Poisson distribution was used for evaluating numbers of deaths among 915 cases of leukemia in the Tokai district of Japan, resulting in a good correlation between theoretical and observed distribution. Field studies on environmental factors demonstrated no common features of high leukemia occurrence. Data pertaining to temporal-spatial interaction were examined from the metropolitan Nagoya area, where there were 169 cases of acute leukemia from 1962-1965. Some evidence of clustering was found, with an excessive number of pairs separated by less than 4 kilometers and 120 days.

70-1677 ACUTE LEUKAEMIA IN NEW ENGLAND. AN INVESTIGATION INTO THE CLUSTERING OF CASES IN TIME AND PLACE. (E.) Merrington, M. (Univ. Coll., London) and C. C. Spicer. Brit. J. Prev. Soc. Med. 23(2):124-127, 1969.

Records of 543 persons who died from acute leukemia in Maine, Massachusetts, New Hampshire and Vermont between 1957-1964 were analyzed by 2 statistical methods (David and Barton method, Knox method) for association of cases in time and place. No clustering of cases was found. The data were limited because dates of onset were not obtainable for 25% of the cases.

70-1678 PATTERNS OF FAMILIAL LEUKEMIA. TEN CASES OF LEUKEMIA IN TWO INTERRELATED FAMILIES. (E.) McPhedran, P. (Yale-New Haven Hosp., Conn.), C. W. Heath, Jr. and J. Lee. Cancer 24(2):403-407, 1969.

In 2 families (total 1205 persons), related through a second-generation marriage and studied through 6-7 generations, 10 persons developed leukemia from 1948-1967. In 1 family, 6 cases

(3 males, 2 females) of chronic lymphocytic leukemia (CLL) occurred in 2 first-cousin sibships (3 in a sibship set of 10 and 3 in a set of 5). In the second family, 4 cases of acute leukemia occurred in a mother, daughter and 2 distant cousins. Cytogenetic studies of peripheral blood lymphocytes from 19 unaffected relatives showed no abnormalities. Among 111 deaths recorded in the families, 10 were due to malignant diseases other than leukemia; anatomic sites included 2 each of liver and lung, and 1 each of throat, testicle, neck, cervix, colon and unspecified site. None of the non-leukemic cancer cases occurred in first-degree relatives of persons with leukemia. It is suggested that familial leukemia is related to cell type, particularly to CLL.

70-1679 HEREDITARY AND FAMILIAL CONSIDERATIONS IN THE STUDY OF ETIOLOGIC FACTORS IN CANCER. (CLINICAL STUDY). (It.) Agresti, A. (U. Naples Inst. Gen. Clin. Surg., Italy), G. Cinque, M. Siciliani and M. De Rosa. Rass. Int. Clin. Ter. 49(8):455-462, 1969.

Among 2500 cancer pts. seen between 1956-1967, inclusive (1324 males, 1176 females; aged 10-85 yr.), the frequency of incidence by age groups rose rapidly between 20-45 yr.; then increased more slowly, peaked at 60 yr., followed by a rapid decline. Cancer in 1 or more blood relatives was reported by 1340/2500, with 822/1340 (62%) reporting cancer in 2-6 siblings, although only 754/1340 reported cancer in a parent, grandparent, child or sibling. Reports of cancer in male relatives exceeded those of cancer in female relatives by 2:1. Among pts. with cancer of the stomach who reported cancer in 1 or more relatives, the cancer in the relative also had a gastric location in 342/663 cases. When the site was extended to include all cancers of the g.i. tract in relatives, the number rose to 414/663. Comparable tabulations among pts. with cancers of the lung were 96/98. Among pts. with cancer of the intestines, they were 46/78, but when the site was extended to include all cancers of the g.i. tract in relatives, the number rose to 108/78, including 52 gastric, 6 esophageal and 4 pancreatic cancers in relatives. The relative percentage of all cancers occurring in the 45-60-yr. age group was higher among pts. with relatives who had cancer than among pts. without family histories of cancer. The situation was reversed, before and after that period.

70-1680 CHILDHOOD CANCER DEATHS IN CALIFORNIA-BORN TWINS. A FURTHER REPORT ON TYPES OF CANCER FOUND. (E.) Norris, F. D. and E. W. Jackson (Bureau Maternal Child Health, Berkeley, Calif.). Cancer 25(1):212-218, 1970.

A study was made of 125,800/145,708 individual twins born in California between 1940 and 1964 who survived to 1 yr. of age. These children

were followed from 1940-1967, during which time there were 54 cases of cancer other than leukemia (33 males and 21 females), with 2 cases still living at the end of 1967. Compared to cancer mortality rates for single-born children, there were 59.3 expected deaths as opposed to 52 observed. The deficit, as with leukemia studies, consisted of females, the second-born and those weighing less than 5.5 pounds at birth. Unlike the leukemia studies, the monozygotic twins had similar observed and expected values, there was an excess of twins dying between 5-14 yr., and there was no independent effect of intra-pair differences in birth wt. Concordant cancer was observed in 3 sets of twins, 2 with leukemia and one with gonadoblastoma.

70-1681 SURVEY OF CANCER IN CHILDREN ADMITTED TO A BRAZILIAN CHARITY HOSPITAL. (E.) Marigo, C. (Santa Casa Misericordia Hosps., Sao Paulo, Brazil), H. Muller and J. N. P. Davies. J. Nat. Cancer Inst. 43(6):1231-1240, 1969.

Childhood malignancies were analyzed in 520 children under 15 yr., admitted to a hospital in São Paulo from 1952-1965 (inclusive). This hospital serves mainly the poorer members of the community; during this period, 80,000 children under 15 were admitted. Of 14,401 children examined histologically and cytologically, 58.1%, 16.7% and 36.3% were 0-4, 5-9 and 10-14 yr. of age, resp. There were 102 cases of leukemia, 103 solid lymphomas, 60 intracranial and spinal tumors, 32 tumors of the sympathetic nervous system, 24 retinoblastomas, 34 nephroblastomas, 35 bone tumors, 33 soft tissue tumors, 26 epithelial tumors, 29 endocrine and gonadal neoplasms, 6 melanomas, 21 teratomas, 11 angiomas and 4 unclassified. Significantly high frequencies of Hodgkin's disease, adrenal cortical tumors and renal carcinomas are noted. It is concluded that such figures for incidence rates vary greatly according to country, and are remarkably high in economically poor areas.

70-1682 EPIDEMIOLOGY OF BONE CANCER IN CHILDREN. (E.) Glass, A. G. and J. F. Fraumeni, Jr. (NCI, Bethesda, Md.). J. Nat. Cancer Inst. 44(1):187-199, 1970.

Death certificates (1,532) of all children under 15 yr. in the U. S. who had died from primary bone cancer during the period 1960-1966 were reviewed, as well as hospital charts (supplied by 12 institutions) of 396 pts. less than 20 yr. old who died from the same disease. Osteogenic sarcoma caused 52% of bone cancer deaths in children less than 15 yr. and 60% of deaths in those from 15-19 yr. of age, whereas Ewing's sarcoma represented 31.8% of deaths in children below age 15 and 30% thereafter. There was an extremely low frequency of Ewing's sarcoma in nonwhite individuals less than 20 yr. of age; among children less than 15 yr., there were 4 observed deaths as

compared to an expected number of 30.8 deaths in males. Similarly, only 5 deaths were seen among nonwhite girls less than 15 yr., as compared to an expected number of 28.6. Girls had a higher mortality at 5-9 yr., but were surpassed by boys at age 13. No significant seasonal variation or time-space clustering was observed. Of 396 pts. in the hospital series, 75 had congenital defects, different tumors or other diseases, including 2 with retinoblastoma. A seemingly higher frequency of tumors of the bone and brain was seen among close relatives.

70-1683 FATAL MELANOMA OF THE LOWER LIMBS AND OTHER SITES: AN EPIDEMIOLOGIC STUDY. (E.) Lee, J. A. H. (U. Washington, Seattle). J. Nat. Cancer Inst. 44(2):257-261, 1970.

Death rates from malignant melanoma in England and Wales during 1958-1967 are reported. In women the lower limb was the primary site; deaths among women rose to a peak at age 40-44 (3.67 times higher than men at this age), declined until age 60-64, and thereafter increased with age. The trend of the death rate with age in women was similar when the period studied was divided into two 5-yr. periods, 1958-1962 and 1963-1967. Males had a lower death rate from melanomas of the lower limb, and did not reach a peak until the sixth or seventh decade. Death rates for all sites other than the lower limb showed no significant difference between men and women. It is suggested that the increased incidence of melanoma in the lower limb of women is due to increased frequency of direct exposure of this area.

70-1684 GEOGRAPHIC PATHOLOGY OF BRAIN TUMORS. 1. DISTRIBUTION OF DEATHS FROM PRIMARY TUMORS. (E.) Kurtzke, J. F. (Georgetown U. Sch. Med., Washington, D. C.). Acta Neurol. Scand. 45(5):540-555, 1969.

Geographical distribution of brain tumors within political subdivisions of Denmark and the U. S. was determined from mortality data. In Denmark, primary brain tumor deaths in 1951 ranged from 37-130% of the national mean annual mortality rate of 5.7/100,000 population; in 1961 the rate ranged from 55-143% of the mean rate of 7.2. There was no evidence of clustering, no significant correlation between the 2 periods and no significant deviation from a homogenous distribution. In the U. S., primary brain tumor deaths ranged from 72-121% of the national mean annual mortality rate of 5.0/100,000 for 1951-1953, and from 73-117% of the national mean of 5.3 for 1961-1963. There was a significant deviation from homogeneity in the first period (6800 annual deaths), but no significant variation in the last period (8400 deaths). High frequency states were found in the northeast and on the west coast, and there was a highly significant association between the distributions for the 2

periods. A significant association was also found between tumor death distribution and that of number of physicians per capita, which was greater for the first period. It is concluded that tumor deaths were uniformly distributed and that the minimal variation is attributable to availability of medical care facilities.

70-1685 NEUROBLASTOMA TRENDS IN TIME. (E.)

Peterson, D. R. (Seattle-King County Dept. Public Health, Seattle, Wash.), A. H. Bill, Jr. and I. S. Kirkland. J. Pediat. Surg. 4(2): 244-249, 1969.

Cases of neuroblastoma from Scotland (119 cases; 1955-1966) and the U. S. and Canada (1251 cases; 1951-1965; data from 25 hospitals) occurred at a fairly constant frequency. There was little evidence for seasonality of occurrence, although this factor is not as well-established as the annual occurrence pattern. Over 30% of cases occurred during the first yr. of life; the proportionate frequency by age group then declined exponentially. Extrinsic environmental factors whose frequency in time show a large wave pattern (epidemic influenza, fallout from bomb testing, etc.) can be excluded as contributing to the genesis of neuroblastoma. The av. incidence rates of neuroblastoma ranged from 5-10 new cases/million children (0-15 yrs. old)/yr.

70-1686 THYROID CARCINOMA IN A KOREAN SURGICAL MATERIAL. WITH REPORT OF A CASE IN A 6-YEAR-OLD GIRL. (E.) Wetteland, P. (Regional Hosp., Linköping, Sweden). Acta Chir. Scand. 135(7):577-584, 1969.

Among all cases of thyroid diseases observed in surgical material in South Korea since 1958, 95/620 (15.3%) were histologically diagnosed as thyroid carcinoma. This represented 0.75% of all neoplasms (3599/5655 neoplasms were malignant) and 0.93% of all cancers found in males; corresponding figures in females were 2.3% and 4.2%, resp. Cancer of the thyroid ranked higher (number 4) in females than in males (number 18) for all malignant neoplasms. No sex difference was evident for age at diagnosis (av. 37.5 yr.). Papillary carcinomas accounted for 68.8% and 87.4% of all carcinomas in males and females, resp. The estimated relative incidence increased sharply to peak within the 30-39-yr. age group, then decreased irregularly; the incidence was low in persons aged 60 yr. or more. Five of the cases in females occurred in individuals less than 20 yr. old, or in 6.3% of the sex-specific total. The case history of a 6-yr.-old girl with papillary carcinoma of ectopic thyroid tissue is presented.

70-1687 CANCER OF THE BREAST IN UTAH. (E.) Fitzpatrick, W. K. (Holy Cross Hosp.,

Salt Lake City, Utah), C. R. Smart and V. Moslander. Rocky Mountain Med. J. 67(1):41-47, 1970.

Analysis was made of 2308 pts. with breast cancer recorded from 1957-1969 in Utah. The largest number of cases (280) was reported in 1968, and gave an incidence rate of 56.2/100,000 females/yr.; the national incidence rate was 60/100,000/yr. There were 21 cases of breast cancer in men. The age of the pts. ranged from 19-95 yr., with a mean age of 55 yr. The age distribution at the time of diagnosis was the same as reported by others, as were incidence, stage at diagnosis and results of treatment. There were 277 (12%) cases with other primary malignancies; the most frequent second primary malignancy was in the opposite breast and accounted for 105 (5%) cases. Seven pts. with 3 primary cancers were recorded.

70-1688 ENVIRONMENTAL AND CONSTITUTIONAL FACTORS IN FEMALE GENITAL CARCINOMA. (Ger.)

Vahrson, H. (U. Giessen Gynec. Clin., Germany). Z. Geburtsh. Gynaek. 172(1):94-106, 1970.

At the gynecology clinic in Giessen, Germany from 1957-1969, treatment of pts. with carcinoma of the cervix (500), ovary (250), uterus (300) and vulva (117) revealed an av. age of 51 yr. (cervix and ovary), 60 yr. (uterus) and 66 yr. (vulva). The youngest pts. were 21, 22, 29, and 35 yr. old, resp. Pts. with carcinoma of the uterus were more overweight and showed a 2-yr. delay in onset of menopause. Parity was highest for women with carcinoma of the vulva (3.06), as compared to carcinoma of the ovary (2.10), uterus (2.45) and cervix (2.85). Diabetes mellitus occurred more frequently in women with carcinoma of the uterus (12.7%) than in pts. with cancer of the cervix (2.6%), ovary (1.6%) or vulva (6.0%). Diabetes seemed to delay the onset of carcinoma, as diabetic women were older than non-diabetic women in all carcinoma groups. It is suggested that endogenous (hormonal) factors are related to the etiology of carcinoma of the uterus.

70-1689 SOME OBSERVATIONS ON CANCER OF THE UTERINE CERVIX IN AFRICANS AND INDIANS OF NATAL. (E.) Schonland, M. (U. Natal, Durban, South Africa) and E. Bradshaw. S. Afr. J. Med. Sci. 34(3):61-71, 1969.

Indians and Africans in Natal have high rates for cancer of the cervix; it accounts for 33% and almost 25% of all malignant growths in the female African and Indian populations, resp. Analysis of 761 cases of cervical cancer for both groups during 1964-1966 showed a mean age for cases of 48 yr. and about 15% were less than 35 yr. old. Circumcision of male partners did not appear to be an effective preventive factor. In a survey of pts. in a family planning clinic, a very high proportion of African females had non-malignant cervical lesions and vaginal discharges

and showed a poor standard of personal hygiene; this was true to a lesser degree among Hindu females. A hospital survey of 250 African and Indian cervical cancer cases and 317 control pts. indicated that those with cancer of the cervix had earlier sex experiences and first pregnancies, and that they were less "westernized" than controls. Indians had earlier menarche and larger families, but exhibited a more stable marital situation than Africans, who showed a large proportion of unmarried women and separated wives.

70-1690 ANALYSIS OF DIFFERENT FACTORS IN WOMEN WITH CARCINOMA OF THE CORPUS UTERI.

(Ger.) Kaiser, R. (U. Munich Gynec. Clin., Germany) and E. Schneider. Zbl. Gynaek. 92(4): 105-110, 1970.

Comparison of data (1957-1966 inclusive) from gynecological clinics in Osaka, Japan and Munich, Germany revealed a 7-fold greater frequency of carcinoma of the uterus and cervix in Munich: 99 uterine carcinomas and 2417 cervical carcinomas, a 1:24.4 ratio (4.1%) in Japan, compared to 1511 and 5078 cases, resp., a 1:3.3 ratio (29.7%), in Germany. While the percentage of carcinomas of the uterus showed no increase in Japan, it rose steadily in Germany (from 22.3% in 1957 to 35.1% in 1966). Comparison of 185 pts. with carcinoma of the uterus to control gynecological pts. of the same age revealed, among the former, a smaller number of deliveries (1.9 and 2.4, resp.); greater frequency of dysfunctional bleeding (30% and 23%, resp.); larger uterus size (av. probe length of 8.2 cm and 7.6 cm, resp.); greater frequency of myomas (25.4% and 15.1%, resp.), benign ovarian tumors (13.8% and 8.1%, resp.) and obesity (70.4% and 51.9%, resp.), especially in those over 60 yr. of age; higher blood pressure, especially in the 56-65-yr. age group; and greater frequency of thromboembolic diseases (65.9% and 46.4%, resp.). It is concluded that the pts. with carcinoma of the uterus have elevated adrenal function which predominates over ovarian function. It is suggested that such hormonal disorders in women of reproductive age could be important (together with genetic predisposition and other factors) in the etiology of carcinoma of the uterus.

70-1691 HEMATOPOIETIC NEOPLASMS OF SLAUGHTER ANIMALS. (E.) Migaki, G. (Armed Forces Inst. Path., Washington, D. C.) Nat. Cancer Inst. Monogr. 32:121-151, 1969.

Material from more than 18,000 cattle, calves (less than 1 yr. old), sheep, goats, pigs, horses and mules was submitted for pathological examination because of clinical signs or lesions at necropsy. From July, 1957-June, 1967, the annual rates of occurrence of malignant lymphomas remained relatively constant in cattle, pigs and sheep, and was very small for goats. Thymomas were observed in 5 species, and mastocytomas and

granulocytic sarcomas only in cattle and pigs. Histology and organ involvement were described.

70-1692 SPONTANEOUS TUMORS IN A COLONY OF *Mystromys albicaudatus* (AFRICAN WHITE-TAILED RAT). (E.) Rantanen, N. W. (Washington State U., Pullman) and B. Highman. Lab. Anim. Care 20(1):114-119, 1970.

Eight spontaneous tumors were found out of a total of 412 necropsies in a large colony of *Mystromys albicaudatus* (African white-tailed rat). Six of the 8 tumors were found in 6 animals over 3 yr. of age, while 2 developed concurrently in an 11-mo.-old animal. The tumors included 1 perianal squamous cell carcinoma, 1 skin adnexal tumor at the elbow, 1 osteosarcoma of the scapula, 1 uterine leiomyosarcoma, 2 hypophyseal adenomas, 1 adenocarcinoma and multiple hepatomas of the liver. No primary tumors have yet been found which involve the lungs or mammary gland in this animal, and this is the first known report on spontaneous neoplasia occurring in this species. It is suggested that this animal may be highly desirable for certain carcinogenic and other experimental studies.

70-1693 PROLIFERATION KINETICS OF AN EXPERIMENTAL ASCITES TUMOUR OF THE MOUSE. (E.) Frindel, E., A. J. Valleron, F. Vassort and M. Tubiana (Gustave Roussy, Inst., Villejuif, France). Cell Tissue Kinetics 2(1):51-65, 1969.

Cell cycles of an NCTC 2472 ascites fibrosarcoma of C3H mice were determined. Contrary to results obtained in solid NCTC 2472 tumors, the duration of the cell cycle and its phases lengthened with the age of the tumor, while the growth fractions remained relatively constant. The first phase to lengthen was G₁; later the durations of the S and G₂ phases also increased. The quantity of DNA/cell was determined by cytospectrophotometry, and this method gave data on the relative number of cells in each phase of the cell cycle during growth.

70-1694 THE CELL CYCLES OF THREE TRANSPLANTABLE MORRIS HEPATOMAS. (E.) Sasaki, T. (Temple U. Sch. Med. Fels Res. Inst., Philadelphia, Pa.), H. P. Morris and R. Baserga. Cancer Res. 30(3):788-793, 1970.

The length of the cell cycle and the growth fraction for each of 3 transplantable rat hepatomas studied *in vivo* were 27 hours and 0.8, resp., for 5123 tc (a fast-growing hepatoma), 49 hours and 0.42 for 7794A (intermediate growth rate), and 234 hours and 0.4 for 7793 (a slow-growing tumor). Cell cycle times of each transplantable hepatoma were similar whether a tumor was grown in the right or left thigh. Each tumor had marked variations in the cell cycle of individual tumor

cells, especially in the G₂ period; the length of G₂ in hepatoma 7793 varied from 5-40 hours.

70-1695 THE NATURAL HISTORY OF CERVICAL CARCINOMA IN SITU. (E.) Green, G. H. (U. Auckland Postgrad. Sch. Obstet. Gynec.) and J. W. Donovan. J. Obstet. Gynaec. Brit. Comm. 77(1):1-9, 1970.

In studies of cervical carcinoma in situ from 1950-1967, 75/576 pts. showed evidence of persistent disease after varied initial treatment; none of these developed invasive cervical cancer during follow-up. Confidence limits were obtained for the probability of carcinoma in situ to become invasive and for the period after which it occurs. Two mathematical models were applied to this problem: a Poisson process model and a fixed-time age-dependent model. These 2 separate assumptions about the distribution of latent periods gave comparable values for these limits, which implied a low invasive potential in conservatively treated carcinoma in situ.

70-1696 SELECTED ASPECTS OF HODGKIN'S DISEASE IN A WHOLE COMMUNITY. (E.) Meytes, D. (Tel Hashomer Govt. Hosp., Israel) and B. Modan. Blood 34(1):91-95, 1969.

Hospital records of all residents of Israel, diagnosed as having Hodgkin's disease during the 5-yr. period from 1960-1964, were reviewed. There were 186 "definite" cases, 169 Jews and 17 Arabs. The minimal mean annual incidence rate was 1.6/100,000, with no significant difference between males and females. When 61 "probable" cases were included, the incidence rate rose to 2.1/100,000. A bimodal incidence was obtained

both for all pts., and for subgroups divided by sex and ethnic origin. There were no significant differences in incidence between various Jewish ethnic groups. Median survival was 27 mo., with a much better prognosis in younger pts. of both sexes and in females younger than 45 yr., as compared to males in the same age group.

70-1697 HODGKIN'S DISEASE IN ISRAEL. (Heb.) Meytes, D. (Tel Hashomer Govt. Hosp., Israel) and B. Modan. Harefuah 76(4):154-157, 1969.

70-1698 COMPARATIVE STUDY OF CARCINOMA OF THE ESOPHAGUS. (E.) Burdette, W. J. (U. Texas M. D. Anderson Hosp. Tumor Inst., Houston). Proc. Amer. Ass. Cancer Res. 10:11, 1969.

70-1699 ARSENIC AS A CAUSE OF RESPIRATORY CANCER IN MAN: AN OCCUPATIONAL STUDY. (E.) Fraumeni, J. F., Jr. (NCI, Bethesda, Md.) and A. M. Lee. Proc. Amer. Ass. Cancer Res. 10:26, 1969.

70-1700 CHILDHOOD LEUKEMIA CLUSTERING? (E.) Glass, A. G. (NCI, Bethesda, Md.) and N. Mantel. Proc. Amer. Ass. Cancer Res. 10:29, 1969.

70-1701 PROTEIN SYNTHESIS AND THE GROWTH KINETICS OF EHRLICH ASCITES TUMOR. (E.) Harris, J. W. (U. California Med. Ctr., San Francisco), F. Meyskens and H. M. Pratt. Proc. Amer. Ass. Cancer Res. 10:35, 1969.

See also abstract nos.: 1444, 1445, 1446, 1447, 1448, 1449, 1450, 1451, 1453, 1455

70-1702 BLASTIC TRANSFORMATION OF LYMPHOCYTES CULTURED IN THE PRESENCE OF A STREPTOCOCCAL ANTIGEN (STREPTOKINASE) AT VARIOUS AGES OF LIFE. (It.) Biscatti, G. (U. Padua Inst. Clin. Pediat., Italy), E. Amirante and M. C. Gasparoni. Boll. Soc. Ital. Biol. Sper. 45(1): 49-50, 1969.

When lymphocytes derived from subjects of varying ages (1 mo. to more than 60 yr.) were incubated with streptokinase, the number of positive stimulated cultures was about 26% during the first 3 mo. of life; increased to about 55% by the end of the first yr.; then stabilized at about 78% by age 5 yr. and older, except for isolated peaks of 86.3% and 87.5%, resp., for the age groups 6-8 yr. and greater than 60 yr. The mean number of stimulated cells per culture was only 15% during the first 3 mo. of life; stabilized at 27% until age 11 yr.; then re-stabilized at about 33% throughout the rest of the life span.

0-1703 EXPERIMENTAL PRODUCTION OF TESTICULAR TERATOMAS IN MICE OF STRAINS 129, A/He, AND THEIR F₁ HYBRIDS. (E.) Stevens, L. C. Jackson Lab., Bar Harbor, Maine). J. Nat. Cancer Inst. 44(4):923-929, 1970.

Testicular teratomas were produced from primordial germ cells in mice of strains 129, A/He and their F₁ hybrids by grafting 12- and 13-day fetal genital ridges into histocompatible testes. In strain A/He, the highest incidence of teratomas (71%) was seen in grafts of 13-day-genital ridges, and the incidence was significantly lower (2-26%) in younger and older grafts. In reciprocal crosses of strains 129 and A/He, the highest incidence of teratomas (97%) occurred in 12-day grafts of 129 x A/He genital ridges, followed by 12-day grafts of A/He x 129 (81%) and 13-day 129 x A/He (35%) genital ridges. Incidence of teratomas in F₁ hybrids was higher when the mother was of strain 129, suggesting a maternal influence on teratocarcinogenesis. It is suggested that 129 x A/He F₁ hybrids and strain A/He mice are useful for studying teratocarcinogenesis because of their high incidence of experimentally-produced teratomas and their very low incidence of spontaneous teratomas.

0-1704 RELATIONSHIP BETWEEN DERMATOMYOSITIS AND MALIGNANT TUMORS. (Ger.) Holzmann, (Johannes Gutenberg U. Derm. Clin., Mainz, Germany) and E. Herz. Arzneimittelforschung (10):335-348, 1969.

233 pts. (126 women, 107 men) with dermatomyositis associated with neoplasms, described in the published literature (182 references) and the authors' pt. group, 191/233 were between 40-70 yr. old (97 were between 40-50). The most frequent tumor was lung cancer (44 men, 8 women),

followed by tumors of the breast, ovary lymph nodes, colon, rectum, uterus, prostate and skin. Most common were carcinomas (204/233; including 48 adenocarcinomas, 41 small cell, 16 squamous cell, 9 scirrhous, 8 polymorphocellular and 78 unclassified carcinomas), followed by reticulum cell sarcomas and melanomas (6 each), Hodgkin's disease (4), lymphosarcoma (3), malignant teratoma (2), leukemia, lymphoblastoma, "endothelial sarcoma," malignant dysgerminoma and myeloma (1 each). Tumors were detected after the onset of symptoms of dermatomyositis in 144/233 and before the onset of dermatomyositis in 46/233; in 27/233, both conditions were detected simultaneously. A valid, positive association between the 2 diseases was not obtained when 12 pts. with dermatomyositis (including 1 with carcinoma) were compared to 36 accident victims. It is suggested that tumors are pathogenetic factors which lead to development of dermatomyositis as a secondary (reaction) disease. The role of immune mechanisms for development of dermatomyositis and its association with malignancy should be regarded as a consequence of tumor development.

70-1705 RISK OF MALIGNANCY IN COLD THYROID NODULES: REPORT OF 607 OPERATED CASES. (Fr.) Mellièrè, D. (Mercy Hosp., Paris), J. P. Massin, C. Calmettes, J.-P. Chigot, J.-C. Savoie and H. Garnier. Presse Med. 78(7):311-314, 1970.

Malignancy developed in 1/71 cystic thyroid nodules which had completely regressed, following aspiration, and in 4/41 which had not. Malignancy was found in 4/15 cold double nodules, 2/38 nodules associated with another nodule or a small goiter, 13/21 which were associated with single lymphadenopathies, 15/17 which were associated with multiple lymphadenopathies, and 76/404 which occurred as isolated nodules. The over-all malignancy rate was about 19%. Increased likelihood of malignancy is suggested when nodules occur in prepubescent children, pts. who have received radiotherapy of the neck, and when nodules are hard and stony, when they create a compression syndrome, or when they are associated with multiple lymphadenopathies. A decreased likelihood of malignancy is suggested when they disappear completely, following aspiration, and when the nodule is associated with a palpable goiter.

70-1706 MAST CELL INCIDENCE AND CELL PROLIFERATION IN THE LYMPHOID ORGANS OF NZB MICE. (E.) Viklický, V. (Inst. Exp. Biol. Genet., Prague) and M. Poláčeková. Folia Biol. (Praha) 15(6):432-438, 1969.

The time relationship between changes in the mast cell (MC) count and the presence of a positive Coombs reaction and proliferative changes in spleen and thymus of 1-17-mo.-old NZB mice were studied. Wt. of thymus, which was greater in

females, decreased with age. Spleen wt. showed no change during the first 5 mo., but increased rapidly from 6 mo. onwards. In Coombs-positive animals, relative spleen wt. was much greater than in negative animals. The proportion of positive Coombs reactions was 31% at 5 mo., 76% at 8 mo. and 100% at 11-17 mo. MC count in the thymus reached a max. at 6 mo.; in the spleen, the MC count was low during the first 5 mo., and increased at 6-8 mo.; being directly correlated with a positive Coombs test. In the thymus, peak MC proliferation occurred with appearance of lymph follicles with germinal centers, and in the spleen with an increase in wt. caused by intensive extramedullary hematopoiesis. Basic histological changes noted in the spleen included hyperplasia of white pulp with hyperreactive germinal centers, marked extramedullary hematopoiesis and proliferation of reticulum cells. It is suggested that changes in MC count are directly correlated to the degree of proliferation of other cell series in the spleen and thymus.

70-1707 KAPOSI'S DISEASE AND CHRONIC LYMPHATIC LEUKEMIA. (It.) Nini, G. and E. Ferrea. (via A. Bosio 28, Rome) G. Ital. Derm. 44-110(2): 89-93, 1969.

A 64-yr.-old man with painful, bilateral xeroderma pigmentosum of the foot and the lower third of the leg, accompanied by bilateral edema of the feet and ankles and by dyspnea on effort, also presented with chronic lymphatic leukemia. Personal and familial history were negative, except for rheumatoid symptoms of some yr. duration, involving the knees and the lumbosacral region. It is suggested that the development of chronic lymphatic leukemia is due to the ability of undifferentiated mesenchyme to evolve pathologically under influence of Kaposi's disease.

70-1708 SERUM LIPOPROTEINS OF RATS BEARING TRANSPLANTED MORRIS HEPATOMA 7777. (E.) Narayan, K. A. (U. Illinois Burnside Res. Lab., Urbana) and H. P. Morris. Int. J. Cancer 5(3):410-414, 1970.

Serum lipoprotein patterns of Buffalo rats bearing Morris hepatoma 7777 were determined 2, 4 and 5 weeks after tumor implantation. A slow-moving, high density lipoprotein (HDL) component, similar to that previously seen in Holtzman rats admin. N-2-fluorenylacetamide (0.03%), was present to a significant extent in hepatoma-bearing rats. At 2 weeks, serum lipoproteins and protein patterns were not significantly different from controls. At 4 weeks, an elevation in all classes of lipoproteins, including HDL, was noted. At 5 weeks, serum lipoproteins were further increased, especially HDL₂. Total serum lipids, cholesterol and phospholipids were considerably increased, while total serum proteins were only slightly elevated in tumor-bearing rats, as compared to controls. A new α_1 -globulin component was seen in serum protein patterns of hepatoma-bearing animals.

70-1709 INFECTIOUS MONONUCLEOSIS: SERIAL HETERO-TRANSPLANTATION OF A CELL LINE ISO-LATED FROM PERIPHERAL BLOOD. (E.) Adams, R. A. (Child. Cancer Res. Found., Boston, Mass.), G. E. Foley, L. Pothier, H. Lazarus and A. Stuart. Proc. Amer. Ass. Cancer Res. 10:2, 1969.

70-1710 CHROMOSOMAL CHARACTERISTICS AND AGGREGATION OF HUMAN PERIPHERAL LEUCOCYTES IN CULTURE AT THE TIME OF ESTABLISHMENT. (E.) Fjelde, A. (Roswell Park Mem. Inst., Buffalo, N. Y.). Proc. Amer. Ass. Cancer Res. 10:25, 1969.

See also abstract nos.: 1454

AUTHOR INDEX

- belson, H. T. 1620
 cheson, E. D. 1658
 dams, R. A. 1709
 garwal, M. K. 1538
 gresti, A. 1679
 hearn, M. J. 1582
 juria, E. 1576
 kamatsu, Y. 1539
 lbert, R. 1560
 lexiandrov, K. 1525
 lli, A. F. 1667
 lthoff, J. 1537
 mbrosioni, J. C. 1632
 mbrus, J. L. 1637
 mes, R. P. 1567,1621
 niel, J. L. 1575
 nirante, E. 1702
 ndervont, H. B. 1599
 nsfield, F. J. 1548
 raki, M. 1477
 rnaud, A. 1482
 shley, D. J. B. 1660,1661
 ssal, N. R. 1648
 uerbach, H. 1543
 zami, M. A. 1536
- agby, S. P. 1622
 ajwa, G. S. 1461
 akke, O. M. 1489
 altimore, D. 1583
 anerjee, M. R. 1623
 arat, N. 1568
 arcellona, P. S. 1463
 arkhudarov, R. M. 1453
 rnowell, E. B. 1623
 rry, E. J. 1540
 rtlett, G. L. 1541
 rserga, R. 1694
 rvetta, L. A. 1461
 ard, J. W. 1577
 nge, M. C. 1479
 nso, L. 1605
 nsted, J. P. M. 1464
 ntley, J. P. 1466
 nyesh-Melnick, M. 1616
 rardet, M. 1575
 rg, J. W. 1665
 rge, T. 1664
 rgs, M. 1598
 rgs, V. V. 1598
 rnard, C. 1624
 nsali, S. K. 1448
 ancifiori, C. 1498,1500
 liczki, F. 1654
 ll, A. H., Jr. 1685
 oron, M. 1624
 scatti, G. 1702
 schoff, F. 1544
 ackham, E. 1586
 air, P. B. 1595,1627
 akeslee, J., Jr. 1643
 ck, F. G. 1542
 eryd, B. 1469
- Bonar, R. A. 1577
 Borisov, B. K. 1453
 Borsos, R. 1578
 Bouroncle, B. A. 1611
 Bowen, J. M. 1625
 Bowman, B. G. 1628
 Brachmann, I. 1478
 Bradshaw, E. 1656,1689
 Braylan, R. C. 1572
 Breedis, C. 1609
 Bresch, H. 1564
 Brown, R. C. 1459
 Brown, R. R. 1484
 Bruchmüller, W. 1670
 Brues, A. M. 1543
 Brunet, M. R. 1605
 Bryan, G. T. 1510,1548,1556
 Bryson, G. 1544
 Buffett, R. F. 1626
 Burdette, W. J. 1698
 Burk, D. 1545
 Burney, S. W. 1484
 Buu-Hoi, N. P. 1546
- Calmettes, C. 1705
 Campbell, W. F. 1579
 Cantaboni, A. 1492
 Cardiff, R. D. 1627
 Carnes, W. H. 1628
 Carri, J. 1669
 Cederqvist, L. 1664
 Ceglowski, W. S. 1571
 Cerilli, G. J. 1472
 Chabot, J. F. 1577
 Chahinian, P. 1451
 Chakrabarty, A. K. 1571
 Chan, P. C. 1513
 Chan, S. P. 1590
 Chandra, S. 1614
 Charney, J. 1593
 Charpin, J. 1482
 Chen, C. C. 1562
 Chermann, J. C. 1569
 Chernina, L. A. 1491
 Chigot, J.-P. 1705
 Chirigos, M. A. 1590
 Chopra, H. C. 1598
 Christie, G. S. 1533
 Chuat, J. C. 1624
 Cinque, G. 1679
 Cioli, V. 1463
 Clapp, N. K. 1547
 Clausen, K. P. 1611
 Codegone, M. L. 1487
 Coezy, E. 1503
 Cohen, S. M. 1510,1548
 Colten, H. R. 1578
 Cousin, J. 1447
 Covelli, V. 1459
 Cowan, D. M. 1523
 Cowdell, R. H. 1658
 Craig, A. W. 1547
 Cremer, N. E. 1629
- Crofton, E. C. 1659
 Cure, S. F. 1629
- Dahme, E. 1519
 Dannenberg, H. 1478
 Daoust, R. 1495,1549
 Darner, E. M. 1611
 Dauber, W. 1530
 Dausset, J. 1437
 Davies, J. N. P. 1681
 Davis, W. C. 1618
 Dawson, P. J. 1630
 Dean, G. 1655
 DeBaun, J. R. 1550
 Defendi, V. 1631,1641
 Degos, L. 1437
 Deinhardt, F. 1584
 DeOme, K. 1622
 DeRoche, G. 1543
 De Rosa, M. 1679
 de-Thé, G. 1632
 De Vaux-St-Cyr, C. 1606
 Diamond, L. 1551
 Dillard, R. D. 1563
 Diosi, P. 1612
 DiPaolo, J. A. 1553
 Dmochowski, L. 1600,1625
 Dobson, R. L. 1466
 Doell, R. G. 1552
 Donovan, J. W. 1695
 Donovan, P. 1553
 Doré, J. F. 1570,1574,1576
 Doré, M. 1576
 Drexler, J. 1485
 Duman, M. 1458
 Dunkel, V. C. 1633
 Dunn, T. B. 1554,1599
 Dunning, W. F. 1558
- Ebert, P. S. 1590,1634
 Eggemann, G. 1670
 Eguchi, M. 1468
 Eilber, F. R. 1591
 Elliott, A. M. 1483
 Ellsworth, P. A. 1634
 Endo, H. 1468
 Epstein, S. S. 1555
 Ershoff, B. H. 1461
 Ertürk, E. 1510,1556
 Evans, A. E. 1566
 Ezdinli, E. Z. 1460
- Fantini, F. 1492
 Fefer, A. 1589,1635
 Feldman, D. G. 1644
 Ferrante, W. A. 1457
 Ferrea, E. 1707
 Ferrer, J. F. 1636
 Fey, F. 1531
 Fiel, R. J. 1637
 Field, J. B. 1461
 Fieldsteel, A. H. 1630

- Fischinger, P. J. 1638
 Fitzpatrick, W. K. 1687
 Fjelde, A. 1710
 Flaks, A. 1462
 Fogh, J. 1604,1639
 Foley, G. E. 1709
 Fong, C. K. Y. 1601,1602
 Forget, A. 1495,1549
 Fournier, A. 1447
 François, D. 1588
 Fraumeni, J. F., Jr. 1682,1699
 Frei, J. V. 1557
 Freytes, M. A. 1669
 Friedell, G. H. 1484,1558
 Friedman, H. 1571,1603
 Friend, C. 1640
 Frindel, E. 1693
 Frolov, A. F. 1619
 Fujimura, S. 1465
 Fukuda, S. 1490
 Furst, A. 1559

 Gaffney, E. V. 1604,1639
 Gallager, H. S. 1600
 Galetti, G. 1492
 Gardner, D. 1560
 Garnier, H. 1705
 Gasparoni, M. C. 1702
 Gaston, M. 1635
 Gautheron, D. 1610
 Gavosto, F. 1446
 Gergely, L. 1617
 Ghittino, P. 1487
 Ghosh, A. K. 1642
 Giao, N. B. 1546
 Gibbs, F. 1636
 Gibson, W. R. 1563
 Girardi, A. J. 1641
 Glass, A. G. 1682,1700
 Goetz, I. E. 1561
 Goldfeder, A. 1642
 Goldman, A. 1513
 Goldner, H. 1603
 Golub, N. I. 1470
 Gott, C. 1582
 Grace, J. T., Jr. 1626,
 1633,1643
 Grande, P. 1668
 Green, G. H. 1695
 Grilli, S. 1524
 Gross, L. 1644
 Grube, D. D. 1543
 Gueguen, S. 1511
 Gutmann, H. R. 1562

 Hagmar, B. 1469
 Hall, W. T. 1592
 Hamilton, J. M. 1462
 Hammond, E. C. 1444
 Hansteen, I.-L. 1514,1515
 Hare, J. D. 1608
 Harris, J. W. 1701
 Harris, P. N. 1563

 Hart, M. L. 1628
 Hartenstein, R. 1534
 Hartmann, P. 1645
 Hata, Y. 1455
 Hayhoe, F. G. J. 1438
 Hays, E. F. 1646
 Heath, C. W., Jr. 1678
 Hecker, E. 1564
 Henderson, J. S. 1565
 Henle, G. 1443
 Henle, W. 1443
 Herz, E. 1704
 Hewetson, J. 1617
 Highman, B. 1692
 Hill, B. R. 1561
 Hirayama, T. 1675
 Hirohata, T. 1662
 Hirose, F. 1672
 Ho, H. C. 1632
 Hochberg, K. 1474
 Holmberg, E. A. D. 1454
 Holzmann, H. 1704
 Horoszewicz, J. S. 1633
 Howard, T. 1545
 Hsiung, G. D. 1601,1602
 Huebner, R. J. 1516,1573,1581
 Hughes, R. G. 1625
 Huguet, J. 1447

 Ikegami, R. 1539
 Invernizzi, F. 1492
 Ishihama, A. 1455
 Israel, L. 1451
 Ito, M. 1508
 Iudicello, P. 1605

 Jackson, E. W. 1680
 Jacquemont, B. 1610
 Jasmin, C. 1569
 Jeejeebhoy, H. F. 1512
 Jenkins, T. W. 1504
 Jensen, F. 1631
 Johansson, H. 1505
 Jolles, B. 1658
 Jones, R., Jr. 1643
 Jull, J. W. 1522
 Jussawalla, D. J. 1448
 Jutz, C. 1546

 Kagabu, T. 1455
 Kaiser, R. 1690
 Kallner, G. 1651
 Karácsonyi, G. 1654
 Karmody, A. J. 1666
 Kashulina, A. P. 1502
 Kayabali, I. 1458
 Keller, A. Z. 1663
 Kelley, N. R. 1449
 Kennedy, J. R. 1483
 Kenzy, S. G. 1618
 King, R. J. B. 1523
 Kinoshita, R. 1561
 Kinzel, V. 1532

 Kirchoff, H. 1479
 Kirkland, I. S. 1685
 Kirsten, W. H. 1566
 Kleihues, P. 1518
 Klein, G. 1617
 Kochen, W. 1474
 Kodama, M. 1507
 Kodama, T. 1507
 Kogure, K. 1465
 Koldovský, P. 1442
 Kourie, F. M. 1650
 Kozlova, A. V. 1452
 Kramarsky, B. 1594,1597
 Krasnow, S. 1647
 Kreider, J. W. 1609
 Krüger, F. W. 1537
 Kudo, N. 1455
 Kunze, E. 1536
 Kuratsune, M. 1662
 Kurtzke, J. F. 1684
 Kutinová, L. 1607
 Kuznetsova, N. N. 1585
 Kwan, H. C. 1632
 Kyle, J. 1666

 Lamotte, G. 1456
 Langlois, A. J. 1577
 Lansing, P. B. 1457
 Lappé, M. A. 1527
 Larson, E. W. 1581
 Lasfargues, E. Y. 1594,1597
 Lasfargues, J. C. 1597
 Lavrin, D. H. 1596
 Lazar, P. 1511
 Lazarus, H. 1709
 Leaf, D. 1562
 Lebreuil, G. 1482
 Ledin, G., Jr. 1559
 Lee, A. M. 1699
 Lee, J. 1678
 Lee, J. A. H. 1683
 LePage, R. N. 1533
 Lesobre, R. 1441
 Levine, A. S. 1579
 Liebelt, A. G. 1622
 Liebelt, R. A. 1622
 Lindeman, R. D. 1648
 Linker-Israeli, M. 1526
 Linnik, A. B. 1470
 Liszczak, T. 1614
 Lora, V. G. 1650
 Lucis, O. J. 1506
 Lucis, R. 1506

 Maass, H. 1652
 Macek, M. 1607
 Mack, J. 1479
 Makino, T. 1455
 Malejka-Giganti, D. 1540
 Malmgren, R. A. 1592
 Manaker, R. A. 1613
 Mandrik, E. V. 1502
 Mantel, N. 1700
 Marczynska, B. 1584

- Marel, A. N. 1453
 Marigo, C. 1681
 Masera, P. 1446
 Massin, J. P. 1705
 Mathé, G. 1436, 1569, 1574
 Matsushima, T. 1475, 1477
 McCombs, R. M. 1616
 McDonough, M. 1494
 McPhedran, P. 1678
 Meier, H. 1516, 1573
 Meltes, J. 1504
 Melliére, D. 1705
 Meranze, D. R. 1494
 Merrington, M. 1677
 Meyskens, F. 1701
 Meytes, D. 1696, 1697
 Midtvedt, T. 1489
 Migaki, G. 1691
 Miller, E. C. 1550
 Miller, J. A. 1439, 1550
 Minaev, A. A. 1481
 Mirand, E. A. 1626
 Mirvish, S. S. 1529
 Miyai, T. 1455
 Modan, B. 1696, 1697
 Mohr, U. 1537
 Mokuno, J. 1676
 Mongin, M. 1482
 Monroe, J. H. 1614
 Moore, D. H. 1593, 1594, 1597
 Mori, T. 1501
 Morris, H. P. 1694, 1708
 Morton, D. L. 1591, 1592
 Morton, J. I. 1580
 Moslander, V. 1687
 Muller, H. 1681
 Myers, B. 1600
 Myers, D. D. 1516, 1573

 Nagai, K. 1501
 Nagayo, T. 1508
 Nakamura, Y. 1455
 Narayan, K. A. 1708
 Neal, J. 1479
 Nelson, R. 1553
 Nini, G. 1707
 Nishimura, R. 1473
 Nishiyama, H. 1673, 1674
 Norris, F. D. 1680

 Ochsner, J. L. 1457
 Oluwasanmi, J. O. 1667
 Ormos, J. 1654
 Ota, K. 1676
 Otsuka, J. 1501

 Pang, E. J. 1566
 Pasqualini, C. D. 1572
 Pauka, B. 1652
 Pauli, A. 1447
 Payan, H. 1482
 Peters, R. L. 1581
 Peterson, D. R. 1685

 Pienta, R. J. 1582
 Pillsbury, N. 1597
 Pinto, J. S. 1466
 Pipkin, G. E. 1473
 Poláčková, M. 1706
 Pothier, L. 1709
 Pratt, H. M. 1701
 Precosta, P. 1610
 Prehn, R. T. 1541
 Price, J. M. 1484, 1548, 1556
 Prodi, G. 1524
 Prough, R. A. 1496
 Provana, A. 1487
 Pry, T. W. 1613

 Rabasa, S. L. 1572
 Rabbat, A. G. 1512
 Rabes, H. 1534
 Rabotti, G. F. 1586
 Rabstein, L. S. 1620
 Raha, C. R. 1528
 Rajewsky, M. F. 1530
 Ramos, L. 1604
 Rantanen, N. W. 1692
 Raphael, B. 1482
 Rapp, H. J. 1578
 Raynaud, M. 1569
 Reed, D. J. 1496
 Refsum, S. B. 1514, 1515
 Reiskin, A. B. 1450
 Reuber, M. D. 1509
 Rigdon, R. H. 1479
 Ritter, F. 1665
 Rocchi, P. 1524
 Röhl, L. 1474
 Rollet, M. 1447
 Rossi, G. B. 1640
 Roth, L. 1612
 Rovera, G. 1446
 Rubin, D. J. 1578
 Rubin, R. C. 1567, 1621
 Rudali, G. 1503
 Ruffino, J. 1441
 Russell, A. 1522

 Saal, F. 1572
 Sachs, H. 1652
 Salomon, J.-C. 1511
 Sandberg, A. A. 1460
 Sarkar, N. H. 1593, 1597
 Sasaki, T. 1694
 Satterfield, L. C. 1459
 Savoie, J.-C. 1705
 Schauer, A. 1497, 1536
 Scher, W. 1640
 Schlegel, J. U. 1473
 Schmähl, D. 1535, 1537
 Schneider, E. 1690
 Schneider, M. 1570, 1574
 Schoentag, R. A. 1601
 Schoental, R. 1464
 Schönebeck, J. 1664
 Schonland, M. 1656, 1689
 Schottenfeld, D. 1665
 Seman, G. 1600

 Shabad, L. M. 1480
 Shamberger, R. J. 1486
 Sharma, J. M. 1618
 Shevliagin, V. Ia. 1585
 Shimkin, M. B. 1494
 Shultz, G. N. 1473
 Siciliani, M. 1679
 Siegel, B. V. 1580
 Silvestrini, B. 1463
 Šimkovič, D. 1587
 Sinkovics, J. G. 1582
 Sivak, A. 1471
 Smart, C. R. 1687
 Smetana, K. 1607
 Smetanin, E. E. 1517
 Smirnov, G. A. 1480
 Smith, G. H. 1599
 Sokal, J. E. 1460
 Spahn, G. J. 1581
 Spicer, C. C. 1677
 Staszewski, J. 1649
 Stavrou, D. 1519
 Steinmuller, D. S. 1527
 Stevens, D. A. 1613
 Stevens, L. C. 1703
 Stockert, J. C. 1454
 Stromberg, K. 1509
 Stuart, A. 1709
 Sugano, H. 1671
 Sugimura, T. 1465, 1477
 Süß, R. 1532
 Svec, F. 1587
 Svec, J. 1587
 Sverak, L. 1577
 Swart, B. E. 1615
 Swern, D. 1494
 Sydow, G. 1531
 Szepsenwol, J. 1493
 Szönyi, F. 1654

 Takahashi, M. 1476
 Takayama, S. 1465
 Tambourin, P. 1568
 Tarnowski, W. M. 1520
 Teichmann, R. 1488
 Terenius, L. 1505
 Thomas, C. 1478
 Thorarinnsson, H. 1653
 Thorén, L. 1505
 Thurzo, V. 1587
 Tiggelbeck, D. 1545
 Toyama, T. 1657
 Trainin, N. 1526
 Treat, R. C. 1472
 Treu-Sarnat, G. 1584
 Troll, W. 1560
 Trujillo, J. M. 1582
 Tubiana, M. 1441, 1693
 Tuczek, H. V. 1534

 Ueda, G. 1501
 Uehleke, H. 1440
 Unakar, N. J. 1467
 Upton, A. C. 1459

Vahrson, H. 1688
Valleron, A. J. 1693
Van Duuren, B. L. 1471
Vassort, F. 1693
Vendrely, C. 1525
Vendrely, R. 1525
Vepřek, L. 1577
Viklický, V. 1706
Völlnagel, T. 1497
Volm, M. 1532
Vonka, V. 1607, 1616

Weinstein, I. B. 1538
Weisburger, J. H. 1499

Welsch, C. W. 1504
Wendling, F. 1568
Wetteland, P. 1686
WHO Expert Committee on Early
Detection of Cancer:
1445
Wieder, R. 1494
Wildanger, F. 1497
Williams, A. O. 1667
Williams, W. C. 1600
Wittkop, J. A. 1496
Wollmann, R. L. 1566
Wynder, E. L. 1513

Yamada, K. 1676
Yamada, S. 1508
Yamamoto, N. 1490
Yamamoto, R. S. 1499
Yanagi, S. 1468
Yata, J. 1617
Young, B. G. 1615

Zador, S. 1521
Zajdel, F. 1568
Závadová, H. 1607

SUBJECT INDEX

- ACETAMIDE, N-4-(4'-FLUOROBIPHENYL)-
liver tumors, age and sex difference, rat:
1509
- ACETAMIDE, N-(4-[5-NITRO-2-FURYL]-2-THIAZOLYL)-
mammary and other tumors, rat: 1510
- ACETYLAMINOFLUORENE (See N-2-Fluorenylacetylamide)
- ACTINOMYCIN D (See under Antitumor agents)
- ADRENAL CORTEX NEOPLASMS
epidemiology, children, Brazil (São Paulo):
1681
- AFLATOXIN B-1
hepatoma, trout: 1487
- AFLATOXIN (aflatoxin analog)
liver, s.c. and intestinal tumors, mouse: 1488
- AGE FACTORS
familial cancer occurrence: 1679
fluorobiphenylacetamide hepatoma, rat: 1509
host immunity
adenovirus-12 or SV40 tumors, hamster:
1603
cancer incidence, review: 1446
leukemia epidemiology, Japan: 1674
mast cell proliferation, NZB mice: 1706
spontaneous remission of Friend viral leukemia,
mouse: 1630
streptokinase-induced lymphocyte transformation,
human: 1702
- AIR POLLUTION
benzpyrene
aircraft exhaust gases and soot: 1480
automobile exhaust gases, engine efficiency
and gasoline quality: 1481
dust and gaseous, cancer epidemiology,
England and Wales: 1660,1661
lung cancer, coal mining and textile-manu-
facturing areas, England and Wales: 1660
stomach cancer, England and Wales: 1661
sulfur dioxide, possible effect on arsenic as
respiratory carcinogen, human: 1699
respiratory diseases, Japan (Tokyo): 1657
- ALDEHYDES AND AMINES, AROMATIC
mechanism of action, review: 1439,1440
- ANTHRACENE, 2-AMINO-
skin tumors, dermal collagen synthesis, rat:
1466
- ANTHRANILIC ACID, 3-HYDROXY-
bladder tumors, hydroxyanthranilic acid
distribution, rat: 1474
and related compound, bladder tumors, effect
of ascorbic acid, mouse: 1473
- ANTIMETABOLITES (See under Antitumor agents)
- ANTITUMOR AGENTS
actinomycin D
effect on erythropoiesis, Friend leukemia
virus-infected mouse: 1568
SV40 transplantation antigen (monkey
cells) and tumor induction (hamster):
1641
actinomycin S or actinomycin D, s.c. sarcoma,
mouse: 1539
antibiotics, effect on surface antigens, EB
virus-positive Burkitt lymphoma cells:
1617
- ANTITUMOR AGENTS (Contd.)
antimetabolites, effect on surface antigens,
EB virus-positive Burkitt lymphoma cells:
1617
asparaginase, effect on Rauscher viral
leukemia, mouse: 1579
complications of therapy, cytomegalovirus
infection, human leukemia: 1612
cyclophosphamide, effect on Moloney viral
sarcoma, mouse: 1589,1635
cytosine arabinoside, effect on SV40 trans-
plantation antigen (monkey cells) and
tumor induction (hamster): 1641
fluorodeoxyuridine, effect on SV40 transplanta-
tion antigen (monkey cells) and tumor
induction (hamster): 1641
hydroxyurea, effect on 2-stage skin
carcinogenesis, mouse: 1513
6-mercaptopurine, leukemogenesis (cell-free
passage of thymic lymphoma), mouse: 1552
6-methylmercaptopurine ribonucleoside, effect
on polyoma virus, mouse embryo cells: 1625
mitomycin C, s.c. sarcoma, mouse: 1539
mutagenic, screening method, mouse: 1555
toyocamycin, effect on avian myeloblastosis
virus in vitro: 1577
- L-ARGININE-L-GLUTAMATE
effect on isoniazid or hydrazine lung tumors,
mouse: 1499
- ARSENIC
occupational exposure, respiratory cancer,
role of air pollution: 1699
- ASBESTOS
occupational exposure, pleural mesothelioma,
case: 1482
- ASCORBIC ACID
effect on
bladder tumor induction, mouse: 1473
skin carcinogenesis, mouse: 1486
- Aspergillus fumigatus
afatoxin, liver, s.c. or intestinal tumors,
mouse: 1488
- AUTOMOBILE EXHAUST (See under Engine exhaust
gases)
- AZOBENZENE, 7,12-DIMETHYL-
liver tumors, liver glycogen, rat: 1549
- AZOBENZENE, 4-DIMETHYLAMINO-
liver tumors
effect of p-hydroxypropiophenone, mouse:
1467
liver glycogen, rat: 1495
muscle-type aldolase activity, rat: 1468
- AZULENO(5,6,7-cd)PHENALENE
s.c. sarcoma, mouse: 1546
- BACTERIA
effect of β -propiolactone: 1490
- BACTERIOPHAGE
DNA, effect of β -propiolactone: 1490
- BENZANTHRACENE
effect on DNA, rat mammary gland, hormone
effects: 1523

BENZANTHRACENE, 7,12-DIMETHYL-

- + croton oil, skin tumors, effect of hydroxy-urea, mouse: 1513
- distribution, dermal mast cells, hairless strain mice: 1520
- effect on
 - DNA, rat mammary gland, hormone effects: 1523
 - RNA, mouse skin: 1525
- mammary tumors
 - isolation of mammary tumor virus, rat: 1598
 - transplantable lines, properties, rat: 1558
- nucleic acid and protein binding, rat tissues: 1524
- ovary tumors, mechanism, mouse: 1522
- skin tumors
 - effect of selenium or vitamin E, mouse: 1486
 - glycolysis and respiration, mouse: 1521

BENZANTHRACENE DERIVATIVES

- ovary tumors, structure-activity relationship, mouse: 1522
- transformation, hamster embryo cells, structure-activity relationship: 1553

BENZENE, HEXAMETHYL-

- skin tumors, mouse: 1478

BENZENESULFONATE, ALKYL-

- g.i. tumor promotion, rat: 1476

1,2-BENZOPYRENE

- effect on RNA, mouse skin: 1525
- distribution, breakdown to metabolites containing K-region, mouse: 1528
- effect on RNA, mouse skin: 1525
- exhaust gases
 - aircraft engines of different types: 1480
 - automobiles, gasoline quality and engine efficiency: 1481
- leukemia, strain differences, mouse: 1479
- metabolism, water-soluble derivatives, hamster embryo cells: 1551
- nucleic acid and protein binding, rat tissues: 1524
- skin tumors, effect of selenium or vitamin E, mouse: 1486

BENZOPYRENE DERIVATIVES

- transformation, structure-activity relationship, hamster embryo cells: 1553

BETEL

- chewing, upper g.i. cancer, Natal (Durban), ethnic groups: 1656

BICYCLO(2.2.0)HEXA-2,5-DIENE, HEXAMETHYL-

- leukemia or liver tumors, mouse: 1478

BLADDER CARCINOGENESIS

- aromatic amines, mechanism, review: 1440
- butyl-N-4-butanolnitrosamine, enzymes, rat: 1536
- dibutylnitrosamine, strain differences, hamster: 1537
- hydroxyanthranilic acid
 - carcinogen distribution, rat: 1474
 - effect of ascorbic acid, mouse: 1473
 - related compound, effect of ascorbic acid, mouse: 1473
- N-(4-[5-nitro-2-furyl]-2-thiazolyl)formamide, rat: 1556

BLADDER NEOPLASMS

- papilloma, risk of malignant transformation, review: 1449

BLOOD

- peripheral WBC cultures
 - chromosomes, normal human: 1710
 - infectious mononucleosis (human), induction of transplantable hamster tumor: 1709

BLOOD DISEASES

- infectious mononucleosis
 - Epstein-Barr virus, review: 1443
 - induction, Epstein-Barr virus (from Burkitt lymphoma cultures), human cancer: 1643
 - peripheral WBC cell line, transplantable hamster tumor (H-RKB2): 1709
 - serum Epstein-Barr virus antibodies: 1613

BLOOD GROUPS

- ABO and Rh, larynx cancer, East Germany: 1670

BLOOD PROTEINS

- lipoproteins and α_1 -globulin, rat with transplanted hepatoma: 1708

BONE

- ^{90}Sr levels, USSR (all ages): 1453

BONE MARROW

- toxicity, methylnitrosourea, mouse: 1557

BONE NEOPLASMS

- epidemiology, children, U.S., ethnic groups: 1682
- radiation-induced (occupational or therapeutic exposure), human: 1452
- sarcoma, serum sarcoma-specific antigens, pts. and their relatives: 1591

BRAIN NEOPLASMS

- epidemiology, geographical variations, Denmark and U.S.: 1684
- induction
 - lipids, mouse: 1493
 - methylnitrosourea, rabbit, enzyme histochemistry: 1519
- methylcholanthrene-induced ependymblastoma, RNA virus-like particles, mouse: 1567, 1621

CARBAMIC ACID, 1,1-DIPHENYL-2-PROPYNYL-N-CYCLOHEXYL

- multiple tumor types, rat, mouse or gerbil: 1563

CARBON TETRACHLORIDE

- effect on liver regeneration, mouse: 1491

CARCINOGENESIS, CHEMICAL

- mechanism, review: 1439
- 4-nitroquinoline-1-oxide and related agents, structure-activity relationship: 1477
- tumor-specific transplantation antigens, review: 1442
- urethan, effect of influenza virus, mouse: 1619

CARCINOGENS, CHEMICAL

- dose-response relationship, mathematical model, animal lung tumors: 1559
- effect on cell growth kinetics, malignant transformation, review: 1450
- mutagenesis, screening method, mouse: 1555
- skin tumors, screening method, mouse: 1463
- transformed hamster embryo cells, LDH isoenzyme patterns: 1561

CELL GROWTH KINETICS

- bronchogenic carcinoma, review: 1451

CELL GROWTH KINETICS (Contd.)

- carcinoma in situ of cervix, human: 1695
- malignant transformation in vitro and in vivo, review: 1450
- methylcholanthrene-induced s.c. sarcoma, mouse: 1514,1515
- mouse ascites fibrosarcoma: 1693
- nucleic acids and enzymes, growing and regressing Moloney viral rhabdomyosarcoma, mouse: 1590
- rat hepatoma
 - cell cycle times and tumor growth rates: 1694
 - effect of hypophysectomy: 1534
- relationship to protein synthesis, mouse tumor: 1701

CERVIX UTERI NEOPLASMS

- carcinoma in situ, growth rate: 1695
- epidemiology
 - Germany (Munich) and Japan (Osaka), hormonal status: 1690
 - intrauterine contraceptive devices, Japan: 1455
 - Natal, ethnic groups: 1689
- induction, hormonal contraceptive, mouse: 1554

CHLOROQUINE

- effect on skin carcinogenesis, mouse: 1486

CHOLESTEROL

- brain tumors, mouse: 1493

CHOLESTEROL PALMITATE POLYMER

- s.c. sarcoma, mechanism, rat: 1544

CHROMOSOMES

- normal human peripheral WBC cultures: 1710
- ³²P-induced mouse leukemia: 1454
- ploidy, tumor growth rate, methylcholanthrene s.c. sarcoma, mouse: 1514
- radiation-induced myeloid leukemia, Hodgkin's disease: 1460
- SV40-transformed human cells: 1607

CLUSTERING (See under Disease outbreaks)

COAL DUST

- air pollution
 - lung cancer, England and Wales: 1660
 - stomach cancer, England and Wales: 1661
- occupational exposure, lung cancer, smoking, Scotland: 1659

COCARCINOGENESIS, CHEMICAL

- alkylbenzenesulfonates, stomach, rat: 1476

COCARCINOGENS, CHEMICAL

- phenols, excretion, germ-free or conventional rats: 1489
- unburned tobacco, skin tumor promoters, mouse: 1542

COLON NEOPLASMS

- polyps
 - risk of malignant transformation, review: 1449
 - smoking: 1485

CONNECTIVE TISSUE NEOPLASMS

- induction, mineral oil, transplantation, mouse: 1492
- liposarcoma, Type C virus-like particles, human: 1592
- sarcoma, serum sarcoma-specific antigens, pts. and their relatives: 1591

CONTRACEPTIVES, HORMONAL

- cervix cancer, mouse: 1554
- estrogen-progestagen type, effect on mammary tumor incidence, mouse: 1503

CONTRACEPTIVES, MECHANICAL

- cervix cancer, Japan: 1455

CORPUS UTERI NEOPLASMS

- epidemiology
 - Germany (Giessen), diabetes and hormonal factors: 1688
 - Japan (Osaka) and Germany (Munich), hormonal factors: 1690

COUMARIN DERIVATIVES

- effect on lung metastases, syngeneic mouse tumors: 1469

CROTON OIL FACTOR A-1

- effect on DNA, RNA and protein, mouse skin: 1564

CROTON OIL PHORBOL ESTERS

- phorbol myristate acetate, effect on RNA, mouse fibroblast line: 1471

CYCLOPHOSPHAMIDE (See under Antitumor agents)

CYTOSINE ARABINOSIDE (See under Antitumor agents)

DIABETES MELLITUS

- association with pancreas cancer, Scotland (northeastern): 1666
- female genital cancer, Germany (Giessen): 1688

DIETARY FACTORS (See also under Foods)

- effect on radiation tumor incidence, mouse: 1461

DISEASE OUTBREAKS

- leukemia clusters
 - California (Los Angeles), children: 1700
 - Japan
 - adults and children, Tokai district: 1676
 - measles, Tokyo and Yugawara, children: 1675
 - New England: 1677

DISEASE TRANSMISSION

- mammary tumor virus, high-tumor (IBA/Gf) to low-tumor (X/Gf) mouse strains, foster-nursing: 1642
- serum sarcoma-specific antigens, sarcoma pts. and their relatives: 1591

DISTRIBUTION

- benzpyrene, metabolites containing K-region, mouse: 1528
- diethylnitrosamine, rat: 1530
- dimethylbenzanthracene, dermal mast cells, hairless strain mice: 1520
- hydroxyanthranilic acid, rat with or without hydroxyanthranilic acid-induced bladder tumor: 1474

DUST

- air pollution, lung or stomach cancer, England and Wales: 1660,1661
- occupational exposure
 - lung cancer, Scotland, smoking: 1659
 - nasal cavity and sinus tumors, shoe manufacturing, England (Northamptonshire), snuff taking: 1658
- soot from exhaust gas, benzpyrene content, Soviet aircraft of different types: 1480

SUBJECT INDEX

EB VIRUS (See under Virus, herpes-type)

EMBRYO

- genital ridge, transplantation, testicular teratoma, mouse: 1703

ENDOCRINE ABLATION

- hypophysectomy
 - effect on cell growth kinetics, induced or transplanted rat hepatoma: 1534
- oophorectomy
 - effect on
 - DNA, hyperplastic alveolar mammary nodules, mouse: 1623
 - hydrazine lung carcinogenesis, mouse: 1498
 - transplanted tumor, mouse: 1507
- orchiectomy
 - effect on
 - hydrazine lung carcinogenesis, mouse: 1498
 - transplanted tumor, mouse: 1507

ENDOTOXIN

- Salmonella typhosa lipopolysaccharide B, enhancement of methylcholanthrene skin tumors, mouse: 1565

ENGINE EXHAUST GASES (See also under Petroleum)

- benzpyrene content
 - airplane engines of different types, USSR: 1480
 - automobile engines, fuel type and engine efficiency, USSR: 1481

ENVIRONMENTAL FACTORS

- air pollution, lung cancer, England and Wales: 1660
- cancer epidemiology, India and other tropical nations, review: 1448
- coal-mining and textile-manufacturing areas, lung cancer, England and Wales: 1660
- g.i. cancer, Oklahoma, ethnic groups: 1648
- geographical variations, brain tumors, Denmark and U.S.: 1684
- industrial and non-industrial regions of city (Hamburg, West Germany), cancer distribution: 1652
- population density, stomach cancer, England and Wales: 1661
- salivary gland tumors, U.S.: 1663
- soil type and rainfall, cancer distribution, U.S.: 1647
- tropical climate, cancer epidemiology, India and other nations, review: 1448

ENZYMES

- aldolase (muscle-type), effect of carcinogens, rat liver: 1468
- antitumor (L-asparaginase), effect on Rauscher viral leukemia, mouse: 1579
- ATPase and acid phosphatase, growing and regressing viral sarcoma, mouse: 1590
- dehydrogenases
 - growing and regressing viral sarcoma, mouse: 1590
 - Rous sarcoma virus-transformed or Rous-associated virus-infected cells: 1588
- DNase and RNase, Friend leukemia virus-infected mouse spleen: 1571
- histochemistry
 - butyl-N-4-butanol-nitrosamine-induced bladder tumors, rat: 1536

ENZYMES (Contd.)

- dimethylhydrazine-induced duodenal tumors, rat: 1497
- pathogenesis of human leukemia, review: 1438
- hydrolases and oxidoreductases, methylnitrosourea-induced brain tumors, rabbit: 1519
- hydroxyacetylaminofluorene sulfotransferase, species difference, liver carcinogen susceptibility, rodent: 1550
- lactate dehydrogenase, isoenzymes, carcinogen-transformed hamster embryo cells: 1561
- mitochondrial, effect of Friend and Rauscher leukemia virus, mouse spleen and liver: 1634
- RNA-dependent DNA polymerase, Rous sarcoma or Rauscher leukemia virus particles: 1583
- thymidine kinase, polyoma virus-induced hamster tumor cells: 1608

EPIDEMIOLOGY

- all tumors
 - Brazil (São Paulo), children: 1681
 - doctors and dentists, South Africa, smoking, ethnic groups: 1655
 - Dominican Republic: 1650
 - India and other tropical nations, review: 1448
 - Israel, ethnic groups: 1651
 - U.S., geographical variations, soil type and annual rainfall: 1647
 - West Germany (Hamburg), industrial and non-industrial areas: 1652
- bone tumors, children, U.S., ethnic groups: 1682
- brain tumors, geographical variations, Denmark and U.S.: 1684
- breast cancer, Utah: 1687
- Burkitt lymphoma, Japan and Okinawa: 1671
- cancer prevention and competitive risks, review: 1444
- cervix cancer
 - Germany (Giessen), diabetes and hormonal factors: 1688
 - intrauterine contraceptive devices, Japan: 1455
 - Japan (Osaka) and Germany (Munich), hormonal factors: 1690
 - Natal, ethnic groups: 1689
- esophagus cancer, U.S. (nonwhite) and Africa (high- or low-cancer nations), smoking and occupation: 1698
- familial cancer, age-, sex- and site-related patterns: 1679
- female genital cancer, Germany (Giessen), diabetes and hormonal factors: 1688
- g.i. cancer, Oklahoma, ethnic groups and environmental factors: 1648
- Hodgkin's disease, Israel, ethnic groups: 1696, 1697
- larynx cancer, blood groups, East Germany: 1670
- leukemia
 - children
 - California (Los Angeles), clusters: 1700
 - Japan: 1673, 1675, 1676

IDEMIOLOGY (Contd.)

clusters

California (Los Angeles), children:

1700

Japan (adults or children): 1675,1676

New England: 1677

familial, cases and review: 1447

Japan, age factors: 1674

multiple-case family (7 generations): 1678

radiation exposure, Hiroshima-Nagasaki:

1672

lip cancer, Italy (Catanzaro and Cosenza Provinces): 1668

lung cancer

Hungary (Szeged), smoking: 1654

Iceland, smoking: 1653

occupational arsenic exposure, air pollution: 1699

Scotland, coal miners, smoking: 1659

South Africa, doctors and dentists, smoking, ethnic groups: 1655

melanoma

Nigeria: 1667

sex difference, England and Wales: 1683

methods

calculation of age-standardized rates for aged: 1649

WHO standards, review: 1445

multiple primary tumors, Sweden (Malmö): 1664

nasal sinus tumors, dust exposure (shoe

manufacturing, bakers' flour) and snuff,

England (Northamptonshire): 1658

neuroblastoma, children, Scotland, U.S. and Canada: 1685

pancreas cancer, diabetes, Scotland (north-eastern): 1666

respiratory diseases, Japan (Tokyo), air pollution and smoking: 1657

salivary gland tumors, environmental factors, U.S.: 1663

second primary tumor, risk, New York: 1665

skin cancer, Nigeria: 1667

⁹⁰Sr levels in bones and teeth, USSR (all ages): 1453

stomach cancer

environmental factors (air pollution, coal and textile industries, socioeconomic

factors), England and Wales: 1661

geographical distribution, relationship to stomach ulcer, Japan: 1662

thyroid cancer, South Korea: 1686

tumors other than leukemia, children, twins, California: 1680

upper g.i. cancer, Natal (Durban), betel chewing, ethnic groups: 1656

uterus cancer

Germany (Giessen), diabetes and hormonal factors: 1688

Japan (Osaka) and Germany (Munich), hormonal factors: 1690

IDEMIOLOGY, VETERINARY

lymphoma, farm animals, U.S.: 1691

spontaneous tumors, colony of *Mystromys**albicaudatus* (African white-tailed rats):

1692

ESOPHAGUS NEOPLASMS

epidemiology

Natal (Durban), ethnic groups, betel

chewing: 1656

U.S. (nonwhite) and Africa (high- or low-cancer nations), smoking and occupation: 1698

familial, siblings: 1669

induction, ethylbutylnitrosamine, rat: 1535

malignant transformation of chemical burn scar: 1457

ESTRADIOL

binding, benign or malignant human breast tumors: 1505

effect on transplanted tumor, sex difference, mouse: 1507

ESTRADIOL DIPROPIONATE

pituitary adenoma, prolactin- and growth hormone-secreting cell types, rat: 1501

ETHNIC GROUPS

bone tumors, children, U.S.: 1682

cancer epidemiology

Israel: 1651

South African doctors and dentists, smoking: 1655

cervix cancer, Natal: 1689

esophagus cancer, U.S. (nonwhite) and Africa (high- or low-incidence regions): 1698

g.i. cancer

environmental factors, Oklahoma: 1648

Natal (Durban), betel chewing: 1656

Hodgkin's disease, Israel: 1696,1697

FATTY ACIDS

s.c. sarcoma, mouse: 1494

FLOUR

occupational exposure, nasal cavity and sinus tumors, England (Northamptonshire): 1658

N-2-FLUORENYLACETAMIDE

binding, transfer RNA, rat liver: 1538

effect on tissue-specific inhibitor of DNA synthesis, rat liver: 1532

liver tumors, cell turnover in early stages, rat: 1560

treated lung explant, s.c. tumors, mouse: 1462

N-2-FLUORENYLACETAMIDE, N-HYDROXY-

binding, liver protein, rat: 1540

liver tumor susceptibility, carcinogen

metabolism, species difference, rodent: 1550

N,N'-2,7-FLUORENYLENEBISACETAMIDE

liver tumors

muscle-type aldolase activity, rat: 1468

radiation enhancement, rat: 1508

FLUORODEOXYURIDINE (See under Antitumor agents)

FOODS (See also Dietary factors)

dimethylamine content, intragastric nitrosamine formation: 1529

FORMAMIDE, N-(4-[5-NITRO-2-FURYL]-2-THIAZOLYL)-

bladder and kidney tumors, rat: 1556

GASTROINTESTINAL CARCINOGENESIS

- dibutylnitrosamine, strain differences, hamster: 1537
- diethylnitrosamine, dose-response relationship, mouse: 1547

GASTROINTESTINAL CARCINOGENESIS

- N-disubstituted arylhydroxylamines, structure-activity relationship, rat: 1562
- ethyl-N'-nitro-N-nitrosoguanidine, rat or mouse: 1464
- intestinal tumors
 - aflatoxin analog (afutoxin), mouse: 1488
 - dimethylhydrazine, enzymes, rat: 1497
 - diphenylpropynyl-N-cyclohexylcarbamate, rat: 1563
 - 2-(2-formylhydrazino)-4-(5-nitro-2-furyl)thiazole and related agents, rat: 1548
 - N-(4-[5-nitro-2-furyl]-2-thiazolyl)acetamide, rat: 1510
- methylnitrosoguanidine, rat or mouse: 1464, 1465
- nitroquinoline oxide, effect of alkylbenzene-sulfonate vehicle, rat: 1476

GASTROINTESTINAL NEOPLASMS

- epidemiology, Oklahoma, ethnic groups and environmental factors: 1648
- familial, age-, sex- and site-related patterns: 1679
- mother and children: 1669
- upper, carcinoma, risk of second primary tumor, New York: 1665

GENETICS, ANIMAL

- age-related spontaneous remission of Friend viral leukemia- BDF₁ mice: 1630
- cancer promotion, review: 1436
- NZB mice, age-related lymphoid mast cell proliferation and autoimmunity: 1706
- strain differences
 - benzpyrene leukemia, mouse: 1479
 - blood mammary tumor virus activity, mouse: 1593
 - dibutylnitrosamine tumor spectrum, hamster: 1537
 - host immunity to Friend leukemia virus, mouse: 1570
 - mammary tumor virus cross-reactivity, mice: 1595
 - Rous viral sarcoma induction, rat: 1585
 - virus-positive or -negative mammary nodules, high- or low-nodule-inducing virus mice: 1622

GENETICS, HUMAN

- albinism, skin cancer, Nigeria: 1667
- cancer promotion, review: 1436
- familial
 - age-, sex- and site-related patterns: 1679
 - esophagus cancer, siblings: 1669
 - leukemia, multiple-case family (7 generations): 1678
 - review: 1437, 1447
- non-leukemic tumors, children, twins, California: 1680

GENITAL NEOPLASMS, FEMALE

- epidemiology, Germany (Giessen), diabetes and hormonal factors: 1688

*GERM-FREE STATUS

- excretion of phenolic cocarcinogens, rats: 1489

GLYCERYL PALMITATE POLYMER

- s.c. sarcoma, mechanism, rat: 1544

HEMATOPOIESIS

- erythropoiesis
 - effect of virus-induced mouse leukemic cell cultures: 1640
 - Friend viral leukemia, mouse: 1568

HEPARIN

- effect on lung metastases, syngeneic mouse tumors: 1469

HEXAMETHYL-DEWAR-BENZENE (See Bicyclo(2.2.0)hexa-2,5-diene, hexamethyl-)

HORMONES (See also Endocrine ablation and specific hormones)

- effect on hydrazine lung carcinogenesis, mouse: 1498
- metabolic status, female genital cancer, Germany (Giessen or Munich) and Japan (Osaka): 1688, 1690
- prolactin and growth hormone, secretion, estradiol-induced pituitary adenoma, rat: 1501

HORMONES, CONTRACEPTIVE

- cervix cancer, mouse: 1554
- estrogen-progestagen type, effect on mammary tumor incidence, mouse: 1503

HORMONES, STEROID

- biosynthesis, spontaneous interstitial cell tumor of testis, mouse: 1506

HORMONES, THYROID

- effect on methylcholanthrene sarcoma, rat: 1502

HYDRAZINE, 1,2-DIMETHYL-

- duodenal tumors, enzymes, rat: 1497

HYDRAZINE, N-METHYL-, DERIVATIVES

- metabolism, rat liver microsomes: 1496

HYDRAZINE SULFATE

- liver tumors (mouse; sex difference) and liver toxicity (hamster): 1500
- lung tumors
 - effect of arginine glutamate, mouse: 1499
 - hormone effects, mouse: 1498

HYDROCORTISONE

- effect on skin carcinogenesis, mouse: 1486

HYDROCORTISONE ACETATE

- effect on transplanted tumor, sex difference, mouse: 1507

HYDROXYLAMINE COMPOUNDS

- N-disubstituted arylhydroxylamines, g.i. tumors, structure-activity relationship, rat: 1562

HYDROXYUREA (See under Antitumor agents)

IMMUNE SERUM

- effect on
 - methylcholanthrene-induced tumors, mouse: 1472, 1512
 - Moloney viral sarcoma, mouse: 1635
 - Rauscher viral leukemia, mouse: 1580
 - transplanted tumors, mouse: 1472

IMMUNE SERUM (Contd.)

- urethan lung carcinogenesis, mouse: 1526
- lung injury, effect on nitroquinoline oxide lung carcinogenesis, mouse: 1475
- pooled human immune globulin, effect on EB virus-infected human leukemia or lymphoma cells: 1615

IMMUNITY

cellular

- mammary tumor virus, strain differences, mouse: 1595
- virus-containing tissues from virus-free mice: 1596
- methylcholanthrene sarcoma, latent period, mouse: 1541
- radiation leukemia virus (rat)-induced lymphoma, mouse or rat: 1628,1636
- Rauscher viral lymphoma cell line, immunoglobulin production: 1582
- soluble or EB viral antigens, serum antibodies, normal children or adults: 1616
- surface antigens
 - carcinogen- or virus-induced mouse leukemias: 1578
 - Epstein-Barr virus-infected cells: 1617,1633
- transplantation immunity
 - effect of antitumor agents, SV40-infected monkey cells: 1641
 - review: 1442
 - SV40 (UV-irradiated)-induced hamster tumors: 1631
- tumor-specific antigens, hamster tumor
 - in vivo or in vitro: 1606

host

- age-related
 - adenovirus-12 or SV40 tumor induction, hamster: 1603
 - cancer incidence, review: 1446
- air pollution (sulfur dioxide and dust) and lung cancer, coal-mining and textile-manufacturing areas, England and Wales: 1660
- cancer promotion, review: 1436
- effect of Friend leukemia virus, sensitive or resistant mouse strains: 1570
- Gross leukemia virus induction, C57BL/6 mice immunized by AKR viral lymphoma: 1575,1576
- human leukemia, review: 1437
- leukemic or preleukemic AKR mice: 1574
- methylcholanthrene sarcoma, latent period, mouse: 1541
- sarcoma-specific antigens, sera from sarcoma pts. and their relatives: 1591
- serum antibodies, avian leukosis-sarcoma group-specific, Rous sarcoma virus-immunized chickens and turkeys: 1586
- soluble and EB viral antigens, normal children or adults: 1616
- serum IgG, Moloney virus-infected rat: 1629

IMMUNITY DISORDERS

- autoimmune hemolytic anemia, lymphoid mast cell proliferation, age factors, NZB mice: 1706
- dermatomyositis, association with cancer, cases and review: 1704

IMMUNOSUPPRESSION

- cyclophosphamide or spleen cells, Moloney sarcoma virus-induced mouse tumors: 1589
- methylcholanthrene, mouse: 1511
- thymectomy, effect on urethan lung carcinogenesis, mouse: 1526
- urethan, mouse: 1527

INJURIES (See also Scar tissue)

- burns, malignant transformation, skin cancer: 1458
- chemical burn, esophagus, malignant transformation: 1457
- lung, antiserum-induced, effect on nitroquinoline oxide lung tumors, mouse: 1475

INSECTICIDES

- mutagenic, screening method, mouse: 1555

ISONICOTINIC ACID HYDRAZIDE

- lung tumors
 - animal and human, review: 1441
 - effect of arginine glutamate, mouse: 1499
- treated lung explant, s.c. tumors, mouse: 1462

KIDNEY CARCINOGENESIS

- 2-(2-formylhydrazino)-4-(5-nitro-2-furyl)thiazole and related compounds, rat: 1548
- N-(4-[5-nitro-2-furyl]-2-thiazolyl)acetamide, rat: 1510
- N-(4-[5-nitro-2-furyl]-2-thiazolyl)formamide, rat: 1556

KIDNEY NEOPLASMS

- epidemiology, children, Brazil (São Paulo): 1681

LACTATION

- mammary tumor virus transmission, high-tumor strain (IBA/Gf) to low-tumor strain (X/Gf) mice: 1642

LARYNX NEOPLASMS

- epidemiology, blood groups, East Germany: 1670

LEATHER

- dust, occupational exposure (shoe manufacturing), nasal cavity and sinus tumors, England (Northamptonshire): 1658

LECITHIN

- brain tumors, mouse: 1493

LEUKEMIA, EXPERIMENTAL (See also under Virus,

- leukemia/lymphoma)
- cell-transmitted, virus particles, guinea pig: 1644
- dimethylbenzanthracene-induced (EL4), cell surface antigens, mouse: 1578
- mouse, virus-induced, cell cultures, erythropoietic activity: 1640

LEUKEMIA, HUMAN

- acute myeloid, EB virus-positive WBC, surface particulate debris: 1614
- cell lines, EB virus-infected, effect of human immune globulin: 1615
- chronic lymphocytic, associated Kaposi's disease of skin, pathogenesis: 1707
- chronic myeloid, irradiated Hodgkin's disease, chromosomes: 1460
- cytomegalovirus infection complicating chemotherapy: 1612

LEUKEMIA, HUMAN (Contd.)

- epidemiology
 - clusters
 - California (Los Angeles), children: 1700
 - Japan, children or adults: 1675,1676
 - New England: 1677
 - Japan, age-related incidence changes: 1674
 - children: 1673,1675,1676
 - radiation exposure (Hiroshima-Nagasaki): 1672
 - familial
 - cases and review: 1447
 - multiple-case family (7 generations): 1678
 - pathogenesis, DNA, RNA and enzyme cytochemistry, review: 1438
 - serum SV40 antibodies, children: 1605
- LEUKEMOGENESIS, EXPERIMENTAL (See also Radiation leukemogenesis, experimental and Virus, leukemia/lymphoma)
 - allogeneic, BALB mice infected with AKR leukemia virus: 1572
 - benzpyrene, strain differences, mouse: 1479
 - diphenylpropynyl-N-cyclohexylcarbamate, mouse, rat or Mongolian gerbil: 1563
 - hexamethylbicyclo(2.2.0)hexa-2,5-diene, mouse: 1478
 - methylcholanthrene or 6-mercaptopurine, cell-free passage of thymic lymphoma, mouse: 1552
 - mineral oil, plasmacytoma or leukemia, transplantable, mouse: 1492
 - splenic lymphosarcoma, N-(4-[5-nitro-2-furyl]-2-thiazolyl)acetamide, rat: 1510
- LEUKEMOGENESIS, HUMAN (See also Radiation leukemogenesis, human)
 - immunity and genetics, review: 1437
- LEUKOSIS, AVIAN
 - skin, herpes-type virus particles, chicken: 1618
- LIP NEOPLASMS
 - epidemiology, Italy (Catanzaro and Cosenza Provinces): 1668
- LIPIDS
 - brain tumors, mouse: 1493
- LIPOPROTEINS
 - serum, rat with transplanted hepatoma: 1708
- LIVER
 - aldolase, effect of carcinogenic or non-carcinogenic compounds, rat: 1468
 - glycogen
 - dimethylaminoazobenzene liver tumors, rat: 1495,1549
 - effect of diethylnitrosamine, sex difference, rat: 1531
 - microsomes, oxidative demethylation of N-methylhydrazines, rat: 1496
 - mitochondrial enzymes, effect of Friend or Rauscher leukemia virus, mouse: 1634
 - protein, hydroxyfluorenylacetamide binding, rat: 1540
 - regeneration, effect of carbon tetrachloride, mouse: 1491
 - tissue-specific inhibitor of DNA synthesis, effect of carcinogens, rat: 1532
 - transfer RNA, fluorenylacetamide binding, rat: 1538

LIVER CARCINOGENESIS

- aflatoxin, trout: 1487
 - afutoxin (aflatoxin analog), mouse: 1488
 - diethylnitrosamine
 - carcinogen activation, rat: 1530
 - cell growth kinetics, effect of hypophysectomy, rat: 1534
 - dose-response relationship, mouse: 1547
 - liver glycogen, rat: 1531
 - dimethylaminoazobenzene
 - effect of p-hydroxypropiophenone, mouse: 1467
 - liver glycogen, rat: 1495,1549
 - dimethylnitrosamine, guinea pig: 1533
 - diphenylpropynyl-N-cyclohexylcarbamate, rat: 1563
 - ethylbutylnitrosamine, rat: 1535
 - fluorenylacetamide, cell turnover in early stages, rat: 1560
 - fluorenylenebisacetamide
 - muscle-type aldolase activity, rat: 1468
 - radiation enhancement, rat: 1508
 - fluorobiphenylacetamide, age and sex difference, rat: 1509
 - 2-(2-formylhydrazino)-4-(5-nitro-2-furyl)thiazole and related agents, rat: 1548
 - hexamethylbicyclo(2.2.0)-hexa-2,5-diene, mouse: 1478
 - hydrazine sulfate, sex difference, mouse: 1500
 - hydroxyfluorenylacetamide, carcinogen metabolism and tumor susceptibility, species difference, rodent: 1550
 - methyltrimethylaminoazobenzene, muscle-type aldolase activity, rat: 1468
- LUNG
- mouse embryo treated with dimethylnitrosamine or methylnitrosourea, adenomatous proliferation, organ culture: 1517
- LUNG CARCINOGENESIS
- dibutylnitrosamine, strain difference, hamster: 1537
 - diethylnitrosamine, dose-response relationship, mouse: 1547
 - dose-response relationship, mathematical model, animal: 1559
 - hydrazine sulfate
 - effect of arginine glutamate, mouse: 1499
 - hormone effects, mouse: 1498
 - isonicotinic acid hydrazide
 - animal and human, review: 1441
 - effect of arginine glutamate, mouse: 1499
 - N-(4-[5-nitro-2-furyl]-2-thiazolyl)acetamide, rat: 1510
 - nitroquinoline oxide, scar tissue, mouse: 1475
 - urethan, effect of immune serum or thymectomy, mouse: 1526
- LUNG NEOPLASMS
- association with dermatomyositis, cases and review: 1704
 - bronchogenic carcinoma, doubling times, review: 1451
 - epidemiology
 - England and Wales, coal mining and textile-manufacturing areas, air pollution: 1660

NG NEOPLASMS (Contd.)

Hungary (Szeged), smoking: 1654
Iceland, smoking: 1653
Japan (Tokyo), air pollution and smoking:
1657
Scotland, coal miners, smoking: 1659
South Africa, doctors and dentists, ethnic
groups, smoking: 1655
familial, age-, sex- and site-related patterns:
1679
risk of second primary tumor, New York: 1665

PHATIC TISSUE

mast cell proliferation, age-related, NZB
mice: 1706
methylnitrosourea toxicity, mouse: 1557
PHOMA, MALIGNANT, EXPERIMENTAL
epidemiology, farm animals, U.S.: 1691
methylcholanthrene- or 6-mercaptopurine-in-
duced, cell-free passage, mouse: 1552
radiation leukemia virus (rat)-induced, virus
particles and antigenicity, rat or mouse:
1628, 1636

thymus graft, Gross leukemia virus-infected
mouse: 1646

PHOMA, MALIGNANT, HUMAN

Burkitt
cells, EB virus-positive, induction of
infectious mononucleosis, human cancer:
1643

surface antigens, effect of antitumor
agents, radiation or cold: 1617
epidemiology, Japan and Okinawa: 1671
Epstein-Barr virus, review: 1443
herpes-type virus-positive WBC, surface
particulate debris: 1614

EB virus-infected cell lines

effect of human immune globulins: 1615
serum antibodies to viral and soluble
antigens, normal children or adults:
1616

Hodgkin's disease

epidemiology
children, Brazil (São Paulo): 1681
Israel, ethnic groups: 1696, 1697
radiation-induced myeloid leukemia,
chromosomes: 1460

pathogenesis, DNA, RNA and enzyme histo-
chemistry, review: 1438

reticulum cell sarcoma, herpes-type virus-
positive WBC, particulate debris on cell
surface: 1614

serum SV40 antibodies, children: 1605

MALIGNANT TRANSFORMATION

burn scar
cancer of esophagus: 1457
skin cancer: 1458

carcinogenic hydrocarbons, structure-activity
relationship, hamster embryo cells: 1553

cell growth kinetics, review: 1450

chemical carcinogens, hamster embryo cells,
LDH isoenzymes: 1561

risk
cold nodules to carcinoma of thyroid: 1705
large intestinal or bladder polyps, review:
1449

MALIGNANT TRANSFORMATION (Contd.)

streptokinase-exposed lymphocytes, age
factors, human: 1702
vaginal pessary implantation, vaginal adeno-
carcinoma: 1456

MAREK'S DISEASE VIRUS (See under Virus, herpes-
type)

MAMMARY CARCINOGENESIS, EXPERIMENTAL (See also
Virus, mammary tumor)
dimethylbenzanthracene, transplantable tumors,
properties, rat: 1558
diphenylpropynyl-N-cyclohexylcarbamate, rat:
1563
2-(2-formylhydrazino)-4-(5-nitro-2-furyl)
thiazole and related agents, rat: 1548
N-(4-[5-nitro-2-furyl]-2-thiazolyl)acetamide,
rat: 1510
pituitary graft, rat: 1504

MAMMARY GLAND

DNA synthesis, effect of benzantracene or
dimethylbenzanthracene, hormone effects,
rat: 1523

MAMMARY NEOPLASMS, EXPERIMENTAL (See also Virus,
mammary tumor)

cells, mammary tumor virus production and
ultrastructure, mouse: 1594
dimethylbenzanthracene-induced, isolation of
mammary tumor virus, rat: 1598
hyperplastic alveolar nodules
DNA, effect of oophorectomy or mammary
tumor virus, mouse: 1623
frequency, high- or low-nodule-inducing
virus mouse sublines: 1622
mouse cell line, stimulation of virus produc-
tion, tissue culture and newborn mouse or
rat: 1597

nodule-inducing virus detection, mammary
tumor virus-free, high-tumor mouse strain:
1599

spontaneous

incidence, effect of estrogen-protestagen
contraceptives, mouse: 1503
virus particles, cat: 1644
transplanted, effect of antilymphocyte serum,
mouse: 1472
transmission, high- to low-tumor mouse strain,
foster-nursing: 1642

MAMMARY NEOPLASMS, HUMAN

benign or malignant, estradiol binding
capacity: 1505
epidemiology, Utah: 1687
mouse leukemia virus-like Type C particles:
1600

6-MERCAPTOPURINE (See under Antitumor agents)

METABOLISM (glycolysis and respiration)
dimethylbenzanthracene skin tumors, mouse:
1521

3-METHYLCHOLANTHRENE

brain tumors, RNA virus-like particles, mouse
1567, 1621
effect on oxidative demethylation of N-
methylhydrazines, rat liver microsomes:
1496
immunosuppression, mouse: 1511
rhabdomyosarcoma (MCG1-SS), effect of anti-
coagulants, mouse: 1469

3-METHYLCHOLANTHRENE (Contd.)

s.c. sarcoma

effect of antilymphocyte serum, mouse:
1472growth rate and latent period, mouse: 1515
and ploidy, mouse: 1514

inhibition by thyroid hormone, rat: 1502

latent period and cellular or host

immunity, mouse: 1541

transplanted, effect of synthetic RNA
polymer, mouse: 1516

promotion by immune serum, mouse: 1512

skin tumors (mouse): 1463

effect of selenium or vitamin E; mouse: 1486

promotion, Salmonella typhosa endotoxin:
1565thymic lymphoma, cell-free passage, mouse:
1552

transformation, hamster embryo cells: 1553

treated lung explant, s.c. tumors, mouse:
14626-METHYLMERCAPTOPYRINE RIBONUCLEOSIDE (See under
Antitumor agents)

MITOMYCIN C (See under Antitumor agents)

MITOSIS

cell cycle times, rat hepatomas of different
growth rates: 1694

MOUTH NEOPLASMS

epidemiology, Natal (Durban), betel chewing,
ethnic groups: 1656

risk, second primary tumor, New York: 1665

MUTAGENESIS

chemical screening method, mouse: 1555

MYELOMA AND RELATED DISEASES

mineral oil plasmacytoma, transplantable,
mouse: 1492

NAPHTHYLAMINES

bladder carcinogenesis, mechanism, review:
1440

NASOPHARYNX NEOPLASMS

cultures, herpes-type virions, Hong Kong
(Chinese): 1632

Epstein-Barr virus, review: 1443

occupational dust exposure (shoe manufacturing
and baking), England (Northamptonshire),
snuff taking: 1658

NEOPLASMS, EXPERIMENTAL

Ehrlich carcinoma (mouse)

cells, bioassay of tobacco smoke: 1545

growth kinetics, protein synthesis: 1701

hyperdiploid or hypotetraploid, hormone
effects, sex difference: 1507epidemiology, colony of Mystromys albicaudatus
(African white-tailed rats): 1692

H-RKB2 (hamster tumor), from peripheral WBC

cell line of human infectious mononucleosis:
1709

immunology and genetics, review: 1436

melanoma B16 (mouse), effect of anticoagulants:
1469Morris 7777 hepatoma (rat), serum lipoproteins
during tumor growth: 1708NCTC-2472 fibrosarcoma (mouse), ascites or
solid, cell growth kinetics: 1693

NEOPLASMS, EXPERIMENTAL (Contd.)

rat hepatomas of different growth rates, cell
cycle times: 1694spontaneous virus-caused tumors, chemotherapy,
mouse: 1573Zajdel hepatoma (rat), cell growth kinetics,
effect of hypophysectomy, rat: 1534

NEOPLASMS, HUMAN

association with dermatomyositis, cases and
review: 1704

epidemiology

age-standardized rate calculation, method,
aged: 1649

children, Brazil (São Paulo): 1681

twins, California: 1680

Dominican Republic: 1650

India and other tropical nations, review:
1448

Israel, ethnic groups: 1651

methods, WHO standards, review: 1445

multiple primary tumors, Sweden (Malmö):
1664South Africa, doctors and dentists, ethnic
groups: 1655U.S., geographical variations, soil type
and annual rainfall: 1647West Germany (Hamburg), industrial and non-
industrial areas: 1652host defense mechanisms and aging, review:
1446

immunology and genetics, review: 1436

infectious mononucleosis induction, Epstein-
Barr virus (from Burkitt lymphoma cell
line): 1643prevention and competitive risks, review:
1444

solid, serum SV40 antibodies, children: 1605

NEUROBLASTOMA

children, epidemiology, Scotland, U.S. and
Canada: 1685

NICOTINAMIDE

metabolites, excretion, smokers: 1484

4-NITROQUINOLINE-1-OXIDE

lung tumors, scar tissue, mouse: 1475

related agents, structure-activity relationship
1477stomach tumors, effect of alkylbenzenesulfonate
vehicle, rat: 1476

NITROSAMINE COMPOUNDS

mechanism of formation in stomach: 1529

NITROSAMINE, N-BUTYL-N-4-BUTANOL

bladder tumors, enzymes, rat: 1536

NITROSAMINE, N-BUTYL-N-ETHYL-

liver or esophagus tumors (benign or malignant)
rat: 1535

NITROSAMINE, DIBUTYL-

respiratory, bladder or g.i. tumors, strain
differences, hamster: 1537

NITROSAMINE, DIETHYL-

distribution, rat: 1530

effect on

liver glycogen, sex difference, rat: 1531

tissue-specific inhibitor of DNA synthesis,
rat liver: 1532

liver tumors

carcinogen activation in liver, rat: 1530

- TROSAMINE, DIETHYL- (Contd.)
 cell growth kinetics, effect of hypophy-
 sectomy, rat: 1534
 lung, liver or stomach tumors, dose-response
 relationship, mouse: 1547
- TROSAMINE, DIMETHYL-
 liver tumors, guinea pig: 1533
 transplacental, effect on embryonic mouse
 lung, organ culture: 1517
- NITROSOGUANIDINE, N-ETHYL-N'-NITRO-
 g.i. tumors, rat or mouse: 1464
- NITROSOGUANIDINE, N-METHYL-N'-NITRO-
 g.i. tumors, rat or mouse: 1464, 1465
- NITROSOUREA, N-METHYL-
 brain tumors, rabbit, enzyme histochemistry:
 1519
 effect on DNA and RNA, rat tissues: 1518
 toxicity, thymus, lymph nodes and bone marrow,
 mouse: 1557
 transplacental, effect on embryonic mouse
 lung, organ culture: 1517
- CLEIC ACIDS, DNA
 benzpyrene or dimethylbenzanthracene binding,
 rat tissues: 1524
 effect of
 benzanthrane or dimethylbenzanthracene,
 hormone effects, rat mammary gland:
 1523
 croton oil factor A-1, mouse skin: 1564
 transplanted or induced hepatoma, rat:
 1534
 methylnitrosourea, rat tissues: 1518
 β -propiolactone, bacteriophage: 1490
- Friend leukemia virus-infected mouse spleen:
 1571
- malignant transformation, review: 1450
- Moloney viral rhabdomyosarcoma, mouse: 1590
- pathogenesis of human leukemia and lymphoma,
 review: 1458
- polyoma virus-induced hamster tumor cells:
 1608
- Shope fibroma virus, isolation and properties:
 1610
- tissue-specific inhibitor from liver, effect
 of carcinogens, rat: 1532
- CLEIC ACIDS, RNA
 carcinogen binding, rat tissues: 1524, 1538
 -dependent DNA polymerase, Rous sarcoma or
 Rauscher leukemia virus particles: 1583
 effect of
 antitumor antibiotic, avian viral leukemic
 WBC: 1577
 carcinogens, mouse skin: 1525
 croton oil fractions, mouse skin or fibro-
 blast cultures: 1471, 1564
 methylnitrosourea, rat tissues: 1518
- Friend leukemia virus-infected mouse spleen:
 1571
- Moloney viral rhabdomyosarcoma, mouse: 1590
- pathogenesis of human leukemia and lymphoma,
 review: 1438
- CLEIC ACIDS, RNA SYNTHETIC POLYMER (polyinosinic-
 polycytidylic acid)
 effect on methylcholanthrene-induced trans-
 planted tumors, mouse: 1516
- OCCUPATIONAL DISEASES
 arsenic exposure, respiratory cancer, possible
 effect of sulfur dioxide air pollution:
 1699
 asbestos exposure, pleural mesothelioma, case:
 1482
 cancer epidemiology
 doctors and dentists, South Africa, smoking:
 1655
 industrial areas of West German city
 (Hamburg): 1652
 dust exposure
 lung cancer, smoking, coal miners, Scotland:
 1659
 nasal cavity and sinus tumors, shoe
 manufacturing or bakery workers, England
 (Northamptonshire): 1658
 esophagus cancer, Africa (high- or low-
 incidence nations) and U.S. (nonwhite):
 1698
 radiation-induced skin, bone or soft tissue
 tumors: 1452
- OIL, MINERAL (See also Petroleum)
 transplantable tumors, pathology, mouse: 1492
- OVARY NEOPLASMS
 human, isolation of chick sarcoma-inducing
 virus from serum or tumor: 1645
 induction, dimethylbenzanthracene and
 metabolites, mechanism, mouse: 1522
- PANCREAS NEOPLASMS
 association with diabetes mellitus, Scotland
 (northeastern): 1666
- PETROLEUM (See also Engine exhaust gases and Oil,
 mineral)
 gasoline, quality, effect on benzpyrene in
 exhaust, Soviet automobiles: 1481
- PHARYNX NEOPLASMS
 epidemiology, Natal (Durban), ethnic groups,
 betel chewing: 1656
- PHENANTHRO(2,1- α)THIAZOLE
 skin tumors, mouse: 1470
- PHENANTHRO(2,1- α)THIAZOLE, 2-METHYL-
 skin tumors, mouse: 1470
- PHENOL COMPOUNDS
 cocarcinogenic, excretion, germ-free or
 conventional rats: 1489
- PHORBOL MYRISTATE ACETATE (See under Croton
 oil phorbol esters)
- PITUITARY
 graft, mammary tumors, rat: 1504
- PITUITARY NEOPLASMS
 estradiol-induced, prolactin- and growth
 hormone-secreting cell types, rat: 1501
- PLASMACYTOMA (See under Myeloma and related
 diseases)
- PLASTICS
 s.c. sarcoma, rat: 1543
- PLEURA NEOPLASMS
 mesothelioma, occupational asbestos exposure,
 case: 1482
- POLYINOSINIC-POLYCYTIDYLIC ACID (See Nucleic
 acids, RNA synthetic polymer)

POLYMERS

cholesterol or glycerol, s.c. sarcoma,
mechanism, rat: 1544

β-PROPIOLACTONE

effect on bacteria and bacteriophage: 1490

PROIOPHENONE, p-HYDROXY-

effect on dimethylaminoazobenzene liver
tumors, mouse: 1467

PROTEINS

carcinogen binding, rat tissues: 1524,1540

PROTEIN SYNTHESIS

effect of croton oil factor A-1, mouse skin:
1564

relationship to growth kinetics, mouse tumor:
1701

PROTOZOA

Tetrahymena pyriformis, effect of tobacco
smoke on mitochondria: 1483

RADIATION CARCINOGENESIS, EXPERIMENTAL

uterus or Harderian gland, effect of diet,
mouse: 1461

RADIATION CARCINOGENESIS, HUMAN

skin, bone or soft tissue, occupational or
therapeutic radiation exposure: 1452
sunlight, skin cancer, albinism, Nigeria:
1667

thyroid, risk, irradiated cold nodules of
thyroid: 1705

RADIATION EFFECTS

enhanced fluorenylenebisacetamide liver tumors,
rat: 1508

surface antigens, EB virus-positive Burkitt
lymphoma cell lines: 1617

RADIATION LEUKEMOGENESIS, EXPERIMENTAL

Moloney or Rauscher virus-like particles,
mouse: 1459

³²P, mouse, chromosomes: 1454

thymic lymphosarcoma, effect of diet, mouse:
1461

RADIATION LEUKEMOGENESIS, HUMAN

Hiroshima-Nagasaki: 1672

Hodgkin's disease, chronic myeloid leukemia,
chromosomes: 1460

RADIOACTIVE ISOTOPES AND ELEMENTS

³²P, mouse leukemia, chromosomes: 1454

⁹⁰Sr, bones and teeth, USSR (all ages): 1453

RECTUM NEOPLASMS

polyps

risk of malignant transformation, review:
1449

smoking: 1485

RESPIRATORY NEOPLASMS

risk of second primary tumor, New York: 1665

RUBBER

dust, occupational exposure (shoe manufacturing),
nasal cavity and sinus tumors, England
(Northamptonshire): 1658

SALIVARY GLAND NEOPLASMS

epidemiology, environmental factors, U.S.:
1663

induction, N-(4-[5-nitro-2-furyl]-2-thiazolyl)
acetamide, rat: 1510

SCAR TISSUE (See also Injuries)

burn scar, malignant transformation, skin:
1458

chemical burn of esophagus, malignant trans-
formation: 1457

lung, antiserum-induced, effect on nitroquinoline
oxide lung tumors, mouse: 1475

vaginal pessary implantation, malignant
transformation: 1456

SELENIUM

effect on skin carcinogenesis, mouse: 1486

SEX DIFFERENCE

familial cancer occurrence: 1679

fluorobiphenylacetamide hepatoma, rat: 1509

hormone responsiveness of transplanted tumor,
mouse: 1507

hydrazine sulfate liver or lung tumors, mouse:
1498,1500

liver glycogen response to diethylnitrosamine,
rat: 1531

melanoma epidemiology, England and Wales:
1683

SKIN

DNA, RNA and protein, effect of croton oil
factor A-1, mouse: 1564

mast cells, dimethylbenzanthracene uptake,
hairless strain mice: 1520

SKIN CARCINOGENESIS

aminoanthracene, dermal collagen synthesis,
rat: 1466

benzpyrene, effect of selenium or vitamin E,
mouse: 1486

dimethylbenzanthracene

+ croton oil, effect of hydroxyurea, mouse:
1513

effect of selenium or vitamin E, mouse:
1486

glycolysis and respiration during tumor
development, mouse: 1521

diphenylpropynyl-N-cyclohexylcarbamate, s.c.
sarcoma or Zymbal's gland tumor, rat:
1563

hexamethylbenzene, mouse: 1478

methylcholanthrene

effect of selenium or vitamin E, mouse:
1486

promotion, Salmonella typhosa endotoxin,
mouse: 1565

N-(4-[5-nitro-2-furyl]-2-thiazolyl)acetamide,
rat: 1510

phenanthro(2,1-α)thiazole and its 2-methyl
analog, mouse: 1470

promotion, unburned tobacco extracts, mouse:
1542

radiation, occupational or therapeutic, human:
1452

s.c. tumors

aflatoxin analog (afutoxin), mouse: 1488

antitumor antibiotics (actinomycins or
mitomycin C), mouse: 1539

azuleno(5,6,7-cd)phenalene, mouse: 1546

carcinogen-treated lung explants, mouse:
1462

cholesterol or glycerol polymers, mechanism,
rat: 1544

fatty acids, mouse: 1494

SKIN CARCINOGENESIS (Contd.)

methylcholanthrene

growth rate and latent period, mouse: 1515

and ploidy, mouse: 1514

latent period and cellular or host

immunity, mouse: 1541

inhibition, thyroid hormone, rat: 1502

promotion, immune serum, mouse: 1512

transplanted, effect of synthetic RNA polymer, mouse: 1516

mineral oil, transplantation, mouse: 1492

plastics, rat: 1543

screening method, mouse: 1463

Shope papilloma virus, mechanism, rabbit: 1609

KIN DISEASES

Kaposi's disease, associated chronic leukemia, pathogenesis: 1707

KIN NEOPLASMS

burn scars: 1458

carcinoma and melanoma, epidemiology, Nigeria: 1667

melanoma, epidemiology, England and Wales, sex difference: 1683

risk, second primary tumor, New York: 1665

OCIOECONOMIC FACTORS

stomach cancer, England and Wales: 1661

OIL

microorganisms, geographical cancer distribution, U.S.: 1647

PLEEN

nuclear size distribution, normal or Friend leukemia virus-infected mouse: 1637

TATOLON

effect on spontaneous virus-induced mouse tumors: 1573

TEARIC ACID DERIVATIVES

s.c. sarcoma, mouse: 1494

OMACH

intra gastric nitrosamine formation from dimethylamine, mechanism: 1529

ulcers, geographical distribution, relationship to stomach cancer, Japan: 1662

OMACH NEOPLASMS

epidemiology

environmental factors, England and Wales: 1661

Japan, air pollution and smoking, Tokyo: 1657

relationship to stomach ulcer, geographical distribution: 1662

Natal (Durban), ethnic groups, betel chewing: 1656

LFUR DIOXIDE

air pollution, effect on arsenic exposure as respiratory carcinogen, human: 1699

20 (See under Virus, adeno-)

40 (See under Virus, papova)

ETH

⁹⁰Sr levels, USSR (all ages): 1453

MPERATURE

low, effect on surface antigens, EB virus-positive Burkitt lymphoma cell lines: 1617

TESTIS NEOPLASMS

spontaneous interstitial cell tumor, steroid biosynthesis, mouse: 1506

teratoma, induction, transplanted embryonic genital ridge, mouse: 1703

TESTOSTERONE

effect on transplanted tumor, sex difference, mouse: 1507

TEXTILES

manufacturing, air pollution, lung cancer, England and Wales: 1660

stomach cancer, England and Wales: 1661

THIAZOLE, 2-(2-FORMYLHYDRAZINO)-4-(5-NITRO-2-FURYL)-

mammary, kidney, liver or g.i. tumors, rat: 1548

THYMUS

graft, lymphoma induction, Gross leukemia virus-infected mouse: 1646

methyl nitrosourea toxicity, mouse: 1557

THYMUS NEOPLASMS

induction, Gross-leukemia virus-infected mouse, thymic graft lymphoma: 1646

6-mercaptopurine-induced lymphoma, cell-free passage, mouse: 1552

methylcholanthrene-induced lymphoma, cell-free passage, mouse: 1552

radiation-induced lymphosarcoma, effect of diet, mouse: 1461

THYROID NEOPLASMS

epidemiology, South Korea: 1686

malignant transformation of cold nodules, risk: 1705

THYRONINE, L-3,5,3'-TRI IODO-

inhibition of methylcholanthrene s.c. sarcoma: 1502

TOBACCO

snuff, nasal cavity and sinus tumors, occupational dust exposure (shoe factory and bakery workers), England (Northamptonshire): 1658

unburned, tumor-promoting substances, mouse skin: 1542

TOBACCO SMOKE

bioassay, method, mouse tumor cell cultures: 1545

effect on mitochondria, Tetrahymena: 1483

TOBACCO SMOKING

effect on excretion of tryptophan and niacin metabolites, human: 1484

esophagus cancer, Africa (high- or low-incidence nations) and U.S. (nonwhite): 1698

lung cancer

Hungary (Szeged): 1654

Iceland: 1653

Scotland, coal miners: 1659

doctors and dentists, South Africa, ethnic groups: 1655

polyps of colon and rectum: 1485

respiratory diseases, Japan (Tokyo): 1657

TOXICITY

hydrazine sulfate, liver, hamster: 1500

methyl nitrosourea, thymus, lymph nodes and bone marrow, mouse: 1557

TOYOCAMYCIN (See under Antitumor agents)

TRACHEA NEOPLASMS

- induction, dibutyl nitrosamine, strain differences, hamster: 1537

TRYPTOPHAN METABOLITES

- excretion, smokers: 1484

URETHAN

- immunosuppression, mouse: 1527
- leukemia, Moloney or Rauscher leukemia virus-like particles, mouse: 1459
- lung tumors, effect of immune serum or thymectomy, mouse: 1526
- skin tumors, mouse: 1463
- treated lung explant, s.c. tumors, mouse: 1462
- tumor induction, effect of influenza virus, mouse: 1619

UTERUS NEOPLASMS (See Corpus uteri neoplasms)

VAGINA NEOPLASMS

- vaginal pessary: 1456

VIRAL CARCINOGENESIS

- tumor-specific transplantation antigens, review: 1442

VIRUS

- foamy type 1 (pseudomyxovirus), fusion of monkey kidney and SV20 adenovirus-induced hamster tumor cells: 1601
- influenza, effect on urethan carcinogenesis, mouse: 1619
- measles, prevalence, leukemia clustering, children, Japan: 1675

VIRUS, ADENO-

- SV20 (simian)
 - abortive or productive infection, monkey or hamster kidney cells: 1602
 - hamster tumors, pathology: 1601
- type 12
 - age-related host immunity and tumor induction, hamster: 1603

VIRUS, HERPES

- cytomegalovirus
 - infection, complication of chemotherapy, human leukemia: 1612
- herpes simplex
 - replication, human lymphocytes: 1611

VIRUS, HERPES-TYPE

- Epstein-Barr (human)
 - Burkitt lymphoma, nasopharynx cancer and infectious mononucleosis, review: 1443
- cell lines
 - Burkitt lymphoma, surface antigens, effect of antitumor agents, radiation or cold: 1617
 - leukemia or lymphoma, effect of human immune globulin: 1615
 - viral and soluble antigens, serum antibodies, normal adults and children: 1616
- induction of infectious mononucleosis, human cancer: 1643
- infected cells, surface antigens: 1633
- particulate debris on surface, WBC from pts. with leukemia or lymphoma: 1614

VIRUS, HERPES-TYPEE (Contd.)

- serum antibodies
 - infectious mononucleosis: 1613
 - normal adults and children: 1616
- human
 - cultures of nasopharynx cancer, Hong Kong (Chinese): 1632
- Marek's disease (avian)
 - isolation, skin leukosis, chicken: 1618
- VIRUS, LEUKEMIA/LYMPHOMA
 - 334C (mouse)
 - effect on Friend virus pathogenicity, mouse: 1626
 - AKR (mouse)
 - allogeneic leukemia induction, BALB mice: 1572
 - chemotherapy of spontaneous leukemias: 1573
 - leukemic or preleukemic mice, host immunity: 1574
 - spontaneous lymphoma, immunization, Gross leukemia virus induction, C57BL/6 mice: 1575, 1576
 - BAL strain A (avian myeloblastosis)
 - leukemic WBC, effect of antitumor antibiotic: 1577
 - Friend (mouse)
 - age-related spontaneous remission, mouse: 1630
 - cell surface antigens: 1578
 - effect on
 - host immunity, sensitive or resistant mouse strains: 1570
 - mitochondrial enzymes, mouse spleen and liver: 1634
 - nucleases and nucleic acids, mouse spleen: 1571
 - erythropoiesis, drug effects: 1568
 - infected spleen, nuclear size distribution, mouse: 1637
 - inhibitor, isolation, Rauscher leukemia virus-infected mouse cell culture: 1569
 - pathogenicity, inhibition by 334C mouse leukemia virus: 1626
 - Gross (mouse)
 - induction, C57BL/6 mice immunized with AKR viral lymphoma cells: 1575, 1576
 - lymphoma induction, thymus graft, mouse: 1646
 - guinea pig
 - cell-transmitted leukemia: 1644
 - Moloney (mouse)
 - helper virus from Moloney sarcoma-leukemia complex, isolation and properties: 1637
 - lymphosarcoma-inducing variant: 1620
 - particles resembling, radiation- or urethan + radiation-induced mouse leukemia: 1459
 - producer rat cell line, effect of extract on Friend viral leukemia (mouse): 1569
 - Moloney leukemia-sarcoma complex (mouse)
 - isolation and properties of helper virus: 1638
 - serum IgG, infected rat: 1629

RUS, LEUKEMIA/LYMPHOMA (Contd.)

- mouse
 - cell-free transmission of methylcholanthrene- or 6-mercaptopurine lymphoma: 1552
 - erythropoietic activity of leukemic cells: 1640
 - particles resembling, methylcholanthrene-induced mouse ependymoblastoma: 1567,1621
 - Type C-like particles, human breast cancer: 1600
- mouse erythroblastosis
 - infection, hemolytic anemia: 1566
- radiation leukemia virus (rat)
 - antigenicity, rat lymphoma: 1628,1636
 - Type C virus particles, mouse or rat lymphoma: 1636
- Rauscher (mouse)
 - cell surface antigens: 1578
 - effect of
 - antitumor enzyme (L-asparaginase): 1579
 - rabbit anti-mouse thymocyte serum: 1580
 - effect on
 - mitochondrial enzymes, mouse spleen and liver: 1634
 - infected mouse cells, isolation of Friend leukemia virus inhibitor: 1569
 - lymphoma cell line (#818), immunoglobulin production: 1582
 - particles resembling, radiation- or urethan + radiation-induced mouse leukemia: 1459
 - RNA-dependent DNA polymerase: 1583
 - survival in atmospheric conditions: 1581
- RPL-12 avian lymphomatosis
 - avian leukosis-sarcoma group-specific antigens, chick embryo cells: 1586

RUS, MAMMARY TUMOR

- cat
 - spontaneous mammary carcinoma or adenocarcinoma: 1644
- human
 - mouse leukemia virus-like Type C particles: 1600
- mouse
 - blood activity, strain differences, mouse: 1593
 - effect on DNA, hyperplastic alveolar nodules, mouse mammary gland: 1623
 - infectivity, assay method, mouse: 1627
 - soluble antigens, virus from different mouse strains: 1595
 - stimulation of production, tissue culture-to-newborn mouse or newborn rat, mouse tumor cell line: 1597
 - tissue immunity, virus-containing tissues of virus-free mice: 1596
 - transmission, foster nursing, IBA/Gf (high-tumor strain) to X/Gf (low-tumor strain): 1642
 - Type A or B particles, methylcholanthrene-induced mouse ependymoblastoma: 1567
 - ultrastructure and production, mammary tumor cell cultures: 1594

VIRUS, MAMMARY TUMOR (Contd.)

- nodule-inducing virus (mouse)
 - detection, mammary tumor virus-free strain and hybrids: 1599
 - high- or low-prevalence mice, hyperplastic alveolar nodule frequency: 1622
- rat
 - isolation (dimethylbenzanthracene-induced tumors) and properties: 1598
- VIRUS, PAPOVA (papilloma-polyoma-vacuolating) polyoma
 - effect of 6-methylmercaptapurine riboside, mouse embryo cells: 1625
 - hamster tumor cells, DNA synthesis and thymidine kinase: 1608
- Shope papilloma (rabbit)
 - skin tumor induction, mechanism, rabbit: 1609
- SV40
 - hamster tumors
 - age-related host immunity: 1603
 - tumor-specific cytoplasmic and perinuclear antigens: 1606
 - transplantation immunity: 1631
 - infected cells, transplantation antigen, effect of antitumor agents: 1641
 - serum antibodies, children with leukemia or solid tumors, polio vaccination: 1605
 - transformed cells
 - human amnion, classification: 1604
 - effect of culture conditions: 1639
 - LEP-12 human diploid cell line, chromosomes and SV40 content: 1607
 - tumorigenicity (hamster), effect of anti-tumor agents: 1641
 - UV-irradiated, hamster tumors, transplantation immunity: 1631
- VIRUS, POX
 - Shope fibroma (rabbit)
 - DNA, isolation and properties: 1610
- VIRUS, SARCOMA
 - human
 - isolation (serum or tumor from women with ovarian tumors) and tumorigenicity (chick): 1645
 - possible, sarcoma-specific antigens, sera from sarcoma pts. and their relatives: 1591
 - Type C particles, liposarcoma culture: 1592
 - Moloney (mouse)
 - effect of cyclophosphamide or immune sera and cells, mouse: 1589,1635
 - replication, human cells (WI-38 cell line): 1624
 - rhabdomyosarcoma, DNA, RNA and enzyme activities, mouse: 1590
 - Moloney sarcoma-leukemia complex (mouse)
 - isolation and properties of helper virus: 1638
 - serum IgG, infected rat: 1629
- mouse
 - lymphosarcoma-inducing variant of Moloney leukemia virus: 1620

SUBJECT INDEX

VIRUS, SARCOMA (Contd.)

- spontaneous tumors, chemotherapy, SJL/J mice: 1573
- Rous-associated (chicken)
 - RAV-1 or RAV-2, infected chick embryo cells, dehydrogenase activities: 1588
- Rous (chicken)
 - Bryan high-titer strain
 - avian leukosis-sarcoma group-specific antigens, infected cells or tumors: 1586
 - Carr-Zilber strain
 - tumor induction, strain differences, rat: 1585
 - Harris strain
 - avian leukosis-sarcoma group-specific antigens, chick embryo cells: 1586
 - immunization, avian leukosis-sarcoma
 - group-specific serum antibodies, chickens or turkeys: 1586
 - RBI rat sarcoma, tumor induction, hamster: 1587

VIRUS, SARCOMA (Contd.)

- RNA-dependent DNA polymerase: 1583
- Schmidt-Ruppin strain
 - avian leukosis-sarcoma group-specific antigens, chick embryo cells or tumors: 1586
 - hamster tumors, avian leukosis-sarcoma virus group-specific antigens: 1586
 - transformed cells
 - chick embryo, dehydrogenases: 1588
 - marmoset, properties: 1584
 - tumor induction, strain differences, rat: 1585

VITAMIN E

- effect on skin carcinogenesis, mouse: 1486

WATER SUPPLY

- annual rainfall, cancer distribution, U.S.: 1647

U.S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
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SEPTEMBER-OCTOBER 1970

Abstract Nos. 1711-2114

Vol. 8
Nos. 9&10

CARCINOGENESIS ABSTRACTS

National Cancer Institute

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE • National Institutes of Health

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Volume 8, Issue 9-10

Abstract Numbers
1711-2114

CONTENTS

	<u>Page</u>
Review	325
Physical Carcinogenesis	329
Chemical Carcinogenesis	333
Viral Carcinogenesis	367
Epidemiology and Biometry	389
Miscellaneous	397
Author Index	i
Subject Index	vi

Prepared by Scientific Literature Corporation
(A Subsidiary of the 3i Company)
Philadelphia, Pennsylvania 19103

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Pursuant to a Contract with the Public Health Service
U.S. Department of Health, Education and Welfare
PH43-70-2036

Use of funds for printing this publication approved
by the Director of the Bureau of the Budget on July 25, 1967.

FOREWORD

The National Cancer Institute, in response to Congressional interest and desire for a national program of cooperative research in cancer, is establishing a means whereby information in the field of carcinogenesis will be coordinated and made available. The information to be included will be obtained from the National Cancer Institute, other governmental agencies, and non-governmental research institutions.

The issuing of Carcinogenesis Abstracts under the auspices of the National Cancer Institute will provide a central source for current abstracting of the carcinogenesis literature being published throughout the world. This will help facilitate an integrated and cooperative program of investigation in this area. The growing number of publications in the area of carcinogenesis makes imperative the availability of an appropriate abstracting service so that investigators may be apprised of progress with a minimum of delay. It is our desire to provide the investigator with a readily systematized compilation of the published work.

Carcinogenesis Abstracts will be published monthly and will include abstracts from the most recently published literature.

Inquiries may be addressed as follows:

Carcinogenesis Abstracts
National Institutes of Health
National Cancer Institute
Bethesda, Maryland 20014

NOTE

Journal names are abbreviated according to the list of abbreviations used by Index Medicus. If the journal is not covered by Index Medicus, then the abbreviations (with some modifications) found in World Medical Periodicals, 3rd Edition, are used.

ABBREVIATIONS USED IN ABSTRACTS

admin.	administered, administration	mg	milligram(s)
av.	average	min.	minute(s)
C	curie(s)	ml	milliliter(s)
mC	millicurie(s)	mm	millimeter(s)
μC	microcurie(s)	mo.	month(s)
cm	centimeter(s)	MTD	maximum tolerated dose
conc.	concentration	NIH	National Institutes of Health, USA
cpm	counts per minute	p.o.	orally
DNA	deoxyribonucleic acid	QO ₂	oxygen quotient
DNase	deoxyribonuclease	PFU	plaque forming unit
e.g.	for example	ppm	parts per million
FFU	focus forming unit	pt.(s)	patient(s)
g.i.	gastrointestinal	RBC	red blood cells (erythrocytes)
g	gram(s)	RES	reticuloendothelial system
μg	microgram(s)	resp.	respectively
Hb	hemoglobin	RNA	ribonucleic acid
i.a.	intra-arterial	RNase	ribonuclease
ID ₅₀	median infectious dose	soln.	solution
inj.	injected, injection(s)	s.c.	subcutaneous
inoc.	inoculated, inoculation(s)	TCID	tissue culture infectious dose
i.p.	intraperitoneal	x	times (e.g. x 3/wk.)
I.U.	international unit(s)	U	unit
i.v.	intravenous	UV	ultraviolet
kg	kilogram(s)	vol.	volume
LD ₅₀	median lethal dose	VA	Veterans Administration
M	molar, mole(s)	wt.	weight
mM	millimole(s)	WBC	white blood cells (leukocytes) or white blood cell count
μM	micromole(s)	yr.	year(s)
max.	maximum		

LANGUAGE ABBREVIATIONS

Af.	Afrikaans	E.	English	Hun.	Hungarian	Lith.	Lithuanian	Ser.	Serbo-Croatian
Ar.	Arabic	Eston.	Estonian	Ic.	Icelandic	Maced.	Macedonian	Sl.	Slovene
Bul.	Bulgarian	Fin.	Finnish	In.	Indonesian	Nor.	Norwegian	Sp.	Spanish
Ch.	Chinese	Fr.	French	It.	Italian	Pol.	Polish	Sw.	Swedish
Cz.	Czech	Ger.	German	Jap.	Japanese	Por.	Portuguese	Th.	Thai
Dan.	Danish	Gr.	Greek	Kor.	Korean	Rum.	Rumanian	Uk.	Ukrainian
Dut.	Dutch	Heb.	Hebrew	Latv.	Latvian	Rus.	Russian	Viet.	Vietnamese

70-1711 EXPERIMENTAL AND ENVIRONMENTAL FACTORS IN CANCER. A REVIEW OF RESEARCH WITH ANIMALS. (E.) LaBarba, R. C. (U. South Florida, Tampa). Psychosom. Med. 32(3):259-276, 1970. (32 references)

A review of animal research relating experiential or environmental factors to the etiology and pathogenesis of neoplastic disease includes studies of crowding, exercise, early experience (handling, immobilization, deprivation, maternal separation), stress (electric shock, avoidance conditioning, fearful exposure), and Soviet research (i.e. the effect of experimentally-induced neurosis on cancer development). The resulting empirical evidence concludes that response to cancer can be influenced by experiential and/or environmental manipulation. Additional research efforts by psychologists are scientifically justified.

70-1712 ORIGIN OF INBRED NZ MOUSE STRAINS. (E.) Bielschowsky, M. (U. Otago, Dunedin, New Zealand) and C. M. Goodall. Cancer Res. 30(3):834-836, 1970. (21 references)

The history and genetic origin of 9 strains of inbred New Zealand mice are described. The characteristics of the strains concerned factors such as obesity, coat color, fostering, possession of a dwarf gene, or the result of cross-breeding between 2 strains. The characteristic diseases of the various strains are reviewed.

70-1713 THE SECOND INTERNATIONAL CONFERENCE ON THE BIOLOGICAL EFFECTS OF ASBESTOS. REPORT ON A VISIT TO EAST GERMANY AND ENGLAND. (E.) Harrington, J. S. (South African Inst. Med. Res., Johannesburg). S. Afr. Cancer Bull. 13(2):60-70, 1969. (No references)

The chemical properties of asbestos fibers and characteristics of asbestos bodies are reviewed in relation to pathogenesis, the carcinogenic properties of asbestos and the epidemiology of asbestosis. The cytotoxic effects of asbestos in industry and mining, and the effect of smoking in the production of asbestosis are discussed.

70-1714 CURE-ALL TO CARCINOGEN. THE PHYSICIAN'S DECISION. (E.) Dilenno, J. (Albert Einstein Med. Ctr., Philadelphia, Pa.). J. Albert Einstein Med. Ctr. (Phila.) 18(1):43-47, 1970. (12 references)

A historical review is presented of the various uses of tobacco. Originally thought to be a panacea (for headaches, tetanus, asthma, etc.), tobacco is now considered a carcinogen.

70-1715 SCIENTIFIC EVIDENCE ON THE ADVERSE EFFECTS OF SMOKING. (Cz.) Horák, J. (City Hosp., Brno, Czechoslovakia). Vnitřní Lek. 15(3):269-282, 1969. (68 references)

The adverse effects of smoking on the respiratory, circulatory and digestive systems are reviewed with particular attention to the association of

lung cancer and smoking. Cancer of the urinary bladder and kidneys, the effects of smoking on vitamin C levels in the blood and blood coagulation, as well as relevant mortality rates, are also discussed.

70-1716 CHROMOSOMAL ABERRATIONS PRODUCED BY CHEMICAL SUBSTANCES. (Fr.) Stahl, A. and J. M. Luciani. Nouv. Rev. Franc. Hemat. 10(1):128-139, 1970. (64 references)

The chromosomal aberrations produced by various chemical substances, with emphasis on the radiomimetic effects of carcinogens and the actions of antibiotics, nitrosamines, methylhydrazines and the carcinogenic substituents of tobacco, are reviewed. Biochemical mechanisms of action, especially inhibition of DNA synthesis and the alteration of its molecular structure, are discussed.

70-1717 CAUSALITY AND MODALITY IN DETERMINING WHETHER SKIN TUMORS ARE AN OCCUPATIONALLY SUSTAINED DAMAGE. (Ger.) Gahlen, W. Arch. Klin. Exp. Derm. 237(1):420-424, 1970.

This review discusses the problems involved in establishing a cause-effect relationship between skin cancer and occupational factors such as tar, arsenic, radiation and trauma. These problems are summarized in relation to claims made for workmen's compensation.

70-1718 HEREDITY OF MALIGNANT MELANOMA. (Cz.) Jílek, M. (Sobeslavská 15, Prague). Cesk. Derm. 44(6):230-234, 1969. (15 references)

The relation of genetic factors and heredity to the etiology of malignant melanoma is reviewed. The results indicate inheritance through a dominant autosomal gene with reduced penetrance. This inheritable melanoma is usually diagnosed at an early age in fair-complexioned, fair-haired, blue-eyed patients who show an increased frequency of multiple primary sites.

70-1719 ON THE EPIDEMIOLOGY OF NASOPHARYNGEAL CARCINOMA. (E.) Clifford, P. (Kenyatta Nat. Hosp., Nairobi, Kenya). Int. J. Cancer 5(3):287-309, 1970. (173 references)

The differences in incidence rates for cancer of the nasopharynx between Chinese populations living in Asia and persons of Chinese descent living under Western-type conditions (Hawaii, Australia, California), and the differences between the incidence rates among Chinese and related Oriental populations (Japanese and Koreans), are interpreted as suggesting that the high incidence of nasopharyngeal cancer among Chinese is the result of environmental factors acting upon a genetically-susceptible population, or to environmental factors alone. It is

suggested that the environmental factors important in the pathogenesis of this tumor may vary from 1 region of the world to another, such as inhalation of polynuclear hydrocarbons in 1 area and ingestion of nitrosamine-like compounds in another region. These external agents may be effective only if combined with a viral infection (the Epstein-Barr virus), or with a particular nutritional or hormonal status which affects the stability of the respiratory epithelium.

70-1720 THE PROBLEM OF POSSIBLE CARCINOGENIC ACTIVITY IN AGENTS USED TO PROTECT PLANTS AND COMBAT PLANT DAMAGE. A DISCUSSION OF THE QUESTION OF OCCUPATIONAL CARCINOGENESIS INDUCED BY SUCH COMPOUNDS, BASED ON CASUISTICS. (Ger.) Gibel, W. (Inst. Cancer Res. Robert-Rossle Clin., Berlin) and K. Lohs. Deutsch. Gesundheits. 24(38):1777-1781, 1969. (77 references)

A review of the carcinogenic and cocarcinogenic activities of organic and inorganic pesticides includes the report of a 35-yr.-old agronomist who developed a spindle-cell adenocarcinoma of the stomach and a metastatic carcinoma of the liver, simultaneously, after more than 20 yr. exposure to a wide range of insecticides, fungicides, and related compounds. No definite correlation has been established between the use of organic insecticides and herbicides and cancer in man although animal experiments suggest such a correlation.

70-1721 ETIOLOGY AND EPIDEMIOLOGY OF CANCER. Heller, J. R. Pp. 3-10 in Gynecological Oncology. A Comprehensive Review and Evaluation, Barber, H. R. K. and E. A. Graber (Eds.). Williams & Wilkins Co., Baltimore, 1969, 386 pp. (13 references)

Ten favorable conditions for the control of cervical cancer are outlined and include the "Pap" smear method and surgery. It is suggested that priority be given to cytological examination of underprivileged women whose high risk of cervical cancer is associated with early marriage and pregnancy. The incidence of uterine cancer among special groups of women such as Catholic nuns, Puerto Ricans, Negroes, Jewish (New York or Israel) and non-Jewish Caucasians, groups of generally low socioeconomic status and inmates of correctional institutions is reviewed. The relation of cervical cancer to male partner circumcision, sexual frequency, age at first coitus, hygiene, sociological status or douche and contraceptive methods is also discussed. A Herpes-type virus origin is suggested for invasive cervical carcinoma; it is possibly transmitted to the cervical area from the smegma of the male at intercourse.

70-1722 CHROMOSOMES IN INVASIVE CARCINOMA AND RELATED LESIONS OF THE UTERINE CERVIX. Wakonig-Vaartaja, T. Pp. 80-88 in Gynecological Oncology. A Comprehensive Review and Evaluation, Barber, H. R. K. and E. A. Graber (Eds.). Williams & Wilkins Co., Baltimore, 1969, 386 pp. (24 references)

Each form of invasive carcinoma of the cervix has a distinct tumor cell line (hyperdiploid) which may be the cause of the invasion. It is suggested that cytogenetic changes in dysplasia are the initial stage of cervical carcinogenesis. During transition from dysplasia to in situ, carcinoma cells with abnormal chromosome numbers and morphology appear.

70-1723 CANCER OF THE BREAST. STATISTICAL AND EPIDEMIOLOGICAL DATA. (E.) Seidman, H. (American Cancer Soc., New York, N. Y.). Cancer 24(6):1354-1378, 1969. (115 references)

Statistical and epidemiological data on the incidence and mortality of breast cancer are discussed with regard to age, sex and ethnic background. The natural history of the disease, long-term survival, clinical and pathological staging, and various methods and results of treatment are also described.

70-1724 URINARY OESTROGEN PROFILES AND AETIOLOGY OF BREAST CANCER. (E.) Smith, O. W. (Boston Hosp. Women, Fearing Res. Lab., Mass.) and G. V. Smith. Lancet 1(7657): 1152-1155, 1970. (19 references)

Discussion of previously published data on the carcinogenicity of estrogen suggests an interaction of the anterior and posterior pituitary hormone in the etiology of breast cancer. Various data on hormone levels and relationships, the role of menopause or oophorectomy and some specific case examples are reviewed.

70-1725 PHYSIOPATHOLOGICAL AND CLINICAL OBSERVATIONS OF HORMONAL BEHAVIOR IN BREAST TUMORS. (It.) Giordano, G. (St. Anna Hosp., Turin, Italy) and P. Cacciari. Arch. Sci. Med. (Torino) 125(10):525-535, 1968. (48 references)

Endocrinology and breast carcinogenesis are discussed in relation to hormonal therapy and its advantages and limitations. Direct therapy (bilateral ovariectomy, adrenalectomy with cortisone, or hypophysectomy) is also discussed in detail; the results of such treatment are considered satisfactory. The effect of the thyroid on breast cancer, analysis of the stages of breast cancer, and schematic treatment plans are also presented.

70-1726 HODGKIN'S DISEASE. (Fr.) Chaudron, J. M. (St. Pierre U. Med. Clin., Louvain, Belgium). Louvain Med. 88(4):337-353, 1969. (73 references)

The incidence rates, etiology, symptoms and disorders associated with Hodgkin's disease are discussed in detail. Included are discussions of laboratory tests, the evolution of the

isease, and statistics of prognosis and survival; the importance of histological examination is stressed.

0-1727 COMBINATION OF HEMOBLASTOSIS AND MALIGNANT TUMOR. NEOPLASTIC TRANSFORMATION AFTER THERAPY OR INTERCURRENT ILLNESS? (Ger.) Reis, H. E. (Ruhr U. Intern. Clin., Essen, Germany), D. K. Hossfeld and H. W. Stier. ad. Welt 20(44):2411-2417, 1969. (42 references)

review of the simultaneous or sequential occurrence of systemic hematologic malignancies with "primary" malignant tumors includes report of 4 cases. A 32-yr.-old man developed chronic myeloid leukemia 2 yr. after unilateral orchiectomy for a non-metastasizing seminoma. A 5-yr.-old woman with chronic lymphatic leukemia of 5 yr. duration developed a metastatic comedo-carcinoma. A 64-yr.-old man with a 9-yr. history of plasmacytoma developed a papillary carcinoma of the bladder. A 70-yr.-old man presented with concurrent plasmacytoma and bronchogenic carcinoma.

0-1728 VIRUSES AND CANCER. Fleissner, E. Pp. 15-20 in Gynecological Oncology. Comprehensive Review and Evaluation, Barber, R. K. and E. A. Graber (Eds.). Williams & Wilkins Co., Baltimore, 1969, 386 pp. (38 references)

types of viruses which cause cancer in animals are reviewed as to their RNA and DNA nature and as to animal susceptibility, resultant tumors and properties of oncogenic transformation. It is postulated that identification of latent viruses in oncogenic viruses may lead to diagnosis, treatment or even prevention of human cancer.

-1729 VIRAL-GENETIC THEORY ON CARCINOGENESIS. EXPERIMENTAL EVIDENCE. (Rus.) Kiselev, L. (Inst. Molec. Biol., Moscow). Vop. Virus. (2):142-149, 1970. (43 references)

the synthesis of complete virus in tumors containing noninfective virus is reviewed. Also discussed is the integration of viral and cell genomes, and the function of viral genomes in cell transformation.

0-1730 CARCINOGENIC ADENOVIRUSES OF HUMAN ORIGIN. (Rum.) Teodosiu, O. (S. S. Nicolau Inst. Inframicrobiol., Bucharest). Stud. Cercet. Inframicrobiol. 20(4):333-343, 1969. (59 references)

the carcinogenic properties of several adenoviruses, which can induce undifferentiated tumors and specific antigens in these tumors, are reviewed in relation to malignant transformation. Although there is no proof of the role of adenoviruses in the etiology of human cancer, inoc. of the adenovirus type 7-SV40 hybrid into monkey renal cell cultures demonstrated that it is the genetic information necessary for the

synthesis of adenovirus type 7 and SV40 T antigens and for the production of malignant transformation and virus replication. It is suggested that the virus is incorporated into the cell in the form of an autonomous nucleic acid, an "infravirus," and that tumors are formed by acquisition of extraneous nuclear material.

70-1731 NUCLEAR ANTIGENS INDUCED IN TUMOR CELLS BY ONCOGENIC DNA VIRUSES. (Rum.) Sahnazarov, N. (S. S. Nicolau Inst. Inframicrobiol., Bucharest). Stud. Cercet. Inframicrobiol. 20(4):303-331, 1969. (154 references)

The antigens produced by oncogenic DNA viruses (those collectively termed T antigens and transplantation antigens) are reviewed. Methods for their detection and differentiation (complement fixation, immunofluorescence, immunodiffusion and absorbed antibody methods, and agglutination reactions) are listed; methods for synthesizing T antigens in cell systems and their characteristics are discussed. The possible nature of the T antigen, as a portion of intracellular virus or as an enzyme necessary for viral replication, is discussed. It is suggested that synthesis of T antigen is dependent on both cellular and viral genomes; as a marker for the adeno-SV40 hybrid virus, it can be used in research of the viral etiology of human cancer.

70-1732 CHROMOSOMAL ANOMALIES IN ANIMAL CELLS FOLLOWING THE ACTION OF DNA TUMOR VIRUSES. (Fr.) Prunieras, M. (A. de Rothschild Found., Paris) and C. Delescluse. Nouv. Rev. Franc. Hemat. 10(1):162-170, 1970. (36 references)

Malignant transformation of different animal cells by DNA tumor viruses in vitro is discussed. Studies showed transformation of embryonic hamster cells by polyoma virus, random chromosome alteration and increased growth induced by SV40 virus, and effects resembling those due to high radiation doses by adenovirus. The karyotypic changes and heteroploid malignancies produced by Shope papilloma virus are also considered. The possibility that fragments of the viral genome become incorporated into the cell genome, leading to alteration of cellular genotype and changes in the rates of DNA synthesis and mitosis, is suggested.

70-1733 CONSTITUTIONAL CHROMOSOMAL ANOMALIES AND LEUKEMIAS. (Fr.) Berger, R. (Inst. Genet., Paris). Nouv. Rev. Franc. Hemat. 10(1):99-107, 1970. (66 references)

The frequency of association of constitutional chromosomal anomalies and leukemias are reported and hypotheses surveyed. The association of trisomy 21 with leukemia, of trisomy 13 with

acute congenital leukemia and partial trisomy D with acute myeloblastic leukemia are given as examples. Familial association of trisomy 21 and other congenital disorders and its more frequent relation to cancer is noted. Different hypotheses to explain these associations are discussed.

70-1734 CHROMOSOMAL ANOMALIES FOLLOWING THE ACTION OF LEUKEMIA VIRUSES IN MICE. (Fr.) Barski, G. (Gustave Roussy Inst., Villejuif, France) and D. Barbieri. Nouv. Rev. Franc. Hemat. 10(1):159-162, 1970. (10 references)

A comparison of spontaneous leukemia in AKR mice and virus-induced leukemia showed no major chromosomal changes for either group. It is suggested, however, that the karyotypic variations found in these 2 cases, although difficult to detect, produce leukemia and that leukemia and these karyotypic variations are separate results of a common underlying pathological process.

70-1735 ELECTRON MICROSCOPIC DEMONSTRATION OF MYELOID LEUKEMIA VIRUS (GRAFFI ET AL.)

IN MICE IN A PRELEUKEMIC STATE. (Ger.) Bierwolf, D. (Inst. Cancer Res., Berlin). Folia Haemat. (Leipzig) 91(2-3):253-259, 1969. (27 references)

The development and spread of virus particles in preleukemic mice of an unspecified strain or strains, following s.c. inj. of ultrasediment from leukemic ascitic fluid or of cell-free filtrates of leukemic organs, are reviewed. Morphologic confirmation of the results of biologic and immunologic studies showing the presence of virus-induced antigens within a few days after inoc. is presented.

70-1736 THE NEWEST DEVELOPMENT OF EXPERIMENTAL INDUCED TUMORS OF THE CENTRAL NERVOUS SYSTEM. (E.) Zülch, K. J. (Max Planck Inst. Brain Res., Cologne-Merheim, Germany). J. Genet. Hum. 17(3/4):511-529, 1969. (79 references)

A review is presented of the newest developments and results of experimentally-produced central nervous system tumors. Terminology, classification and grading of brain tumors and their degree of malignancy are discussed.

See also abstract nos: 2071

70-1737 PHYSICAL AGENTS AS CAUSATIVE FACTORS OF CERVICAL CARCINOMA. Kaminetzky, I. A. Pp. 11-14 in Gynecological Oncology. A Comprehensive Review and Evaluation, Barber, I. R. K. and E. A. Graber (Eds.). Williams & Wilkins Co., Baltimore, 1969, 386 pp.

Some physical agents though to be causative factors of cervical carcinoma are briefly discussed and include: the traumas of pregnancy, repeated labors and births, sexual frequency and ionizing radiation. One possible relation of trauma to carcinogenesis is that following epithelial destruction there is rapid cell proliferation involving many mitotic incidents, and epithelial cells are especially likely to incorporate carcinogenic substances during this process. Possibly, the metabolic processes associated with mitosis are more vulnerable in this regard than are those related to cell maturation following mitosis. Estrogen, being a mitotic stimulator, enables rapid incorporation of carcinogenic substances. It is concluded that the physical agents involved in the carcinogenic process are only links in an extensive chain leading to malignancy.

70-1738 TRAUMA AND BRAIN TUMOR. (Cz.) Kokavec, M. (U. Komenskeho Fac. Med., Bratislava, Czechoslovakia), D. Bartko and V. Korman. Bratisl. Lek. Listy 52(5):581-589, 1969.

A 15-yr.-old boy with a history of resuscitation at birth and brain concussion as a child, developed brain contusions as a result of a rather severe accident involving the head; he died after 5 mo. with intracranial hypertension. Autopsy showed histology characteristic of glioblastoma. It is concluded that repeated trauma, particularly of a previously-damaged area, can lead to malignant growth.

70-1739 MALIGNANT TRANSFORMATION OF LESIONS PRODUCED BY THE USE OF TOTAL UPPER PROSTHESES WITH SUCTION CHAMBERS. (Por.) Garrafa, V. (San Paulo Cancer Assoc. Cent. Inst., Brazil) and D. dos Santos Pinto. Rev. Bras. Cirurg. 58(3-4):303-311, 1969.

In a study of malignant tumors of the hard palate, 8/146 (5.48%) cases were attributed to suction chamber trauma involving total upper prostheses; 5 occurred in women and 3 were in men aged 20-72 yr. The greatest tumor development involved the median region of the hard palate with some instances of invasion of deep osseous layers. Cervical lymph node metastasis was suspected in 5 pts., and in 2/3 extirpation of lymph nodes revealed metastases. Of the 8 cases, one pt. had adenocarcinoma and was treated electrosurgically, but died 12 mo. later with no signs of tumor; the other 7 were cases of

spinocellular carcinoma. Of these pts., 2/7 had invasion of the ethmoid process and nasal fossae which resisted treatment and they died within 7 mo. Radioactive molding placed on the hard palate (7 hours/day x 8 days; total 6000 r) was used in treatment of 4/7 pts.; 2 were free of symptoms after 180 mo., 1 after 117 mo. and 1 after 7 mo. The final pt. was treated by contact radiotherapy (total 7200 r) had remained asymptomatic after 166 mo.

70-1740 CARCINOMA ARISING IN SCAR TISSUE - A TOO-RARE DIAGNOSIS. (Ger.) Pierer, H. (Graz U. Surg. Clin., Austria). Langenbecks Arch. Chir. 324(4):315-332, 1969.

Between 1957-1968, inclusive, 47 carcinomas arising in scar tissue were treated at the Graz University surgical clinic. Included (mean latency period in parentheses, followed by range) were 7 in scars due to burns (44 yr.; 7-67 yr.), 8 in scars due to wounds (29 yr.; 20-45 yr.), 9 in scars due to chronic ulceration (31 yr.; 15-44 yr.); 8 in fistulae (35 yr.; 19-47 yr.), 12 following therapeutic radiation (25 yr.; 7-40 yr.) and 3 due to occupational exposure to radiation (all carcinomas of the hand, in 3 physicians). One fibrosarcoma following radiotherapy was also treated. The incidence of malignancy among all pts. with radiation damage to the skin was 16%. All carcinomas in burn scars were in contractures which impeded joint motility. Half the carcinomas in wound scars were found on the sole of the foot; the remainder were in parts of the body exposed to chronic irritation or repeated, minor injuries. Surgical removal of the tumor was possible in 35/46 pts. who were operated; 11/46 required amputation. Prognosis for these types of tumor is considered uniformly unfavorable, and the importance of early diagnosis and prophylactic treatment in areas of scarification is stressed.

70-1741 LATE CARCINOGENESIS OF A SCARIFIED ESOPHAGEAL STENOSIS. (Fr.) Chassagnon, C. (Jules Courmont Hosp., Pierre Benite, France), J. Rechatin and E. Saubier. J. Med. Lyon 51(1182):681-683, 1970.

A 42-yr.-old man was treated for relapse of a difficult esophageal passage. At age 4.5 yr. he had accidentally swallowed lye; this was followed by progressive dysphagia which required dilatation of the stomach cardia and esophagus at various occasions up to age 27 yr. There was no treatment from age 27-42 yr., when dilatation was unsuccessful. Antibiotic treatment was also necessary then for pulmonary infection, and difficulty in swallowing and breathing continued. Biopsy confirmed keratinizing spinocellular epithelial carcinoma of the scarified esophageal stenosis. Esophagectomy

was performed to remove the large, hardened tumor adhering to the aorta, but relapse occurred after 6 mo. The importance of the time lapse between original scarification and carcinogenesis and the possible traumatic effect of esophageal dilatation on hardened tumor, in conjunction with infection, is considered.

70-1742 GENETICS AS GUIDE TO EARLY DIAGNOSIS AND CANCER CONTROL - CUTANEOUS SYNDROMES.

(E.) Lynch, H. T. (Creighton U. Sch. Med., Omaha, Neb.) and J. Szentivanyi. Cutis 6(2):179-185, 1970.

A listing of inherited disorders with cutaneous symptoms and possible development of carcinoma is presented. Xeroderma pigmentosum (XDP), which is an autosomal recessive disorder, is discussed and a family case history is presented. In the family, 2 females and 3 males (including twins) were diagnosed as having XDP as a result of research by a physician knowing the genetic origin of the disorder. Methods of cancer control and protection, including education of the general population and genetical review in families with cancer occurrences, are suggested.

70-1743 SKIN CARCINOMA RESULTING FROM RADIATION DERMATITIS. (Rum.) Vulcan, P.

(Dermatovener. Clin. IIa, Bucharest, Rumania) and V. Neaga. Derm.-Vener. (Buc.) 14(4):297-302, 1969.

Over a 13-yr. period, 40 cases of skin carcinoma due to radiotherapy (800-1200 r) for various cutaneous or visceral conditions such as eczema, psoriasis, mycosis, hypertrichosis of the face or abdominal and uterine cancer, were reported after a latent period of 5-40 yr. Skin carcinomas included 23 basal cell, 13 spinocellular and 4 undifferentiated or mixed types.

70-1744 EFFECT OF GAMMA-IRRADIATION ON TUMOR INDUCTION BY ULTRAVIOLET RAYS. (Rus.)

Sviderskaia, T. A. (Sci. Res. Inst. Radiation Hyg., Leningrad, USSR), S. N. Alexandrov and A. V. Gubareva. Vop. Onkol. 15(3):83-87, 1969.

Carcinogenic effects of UV (total 25,600 watt/min./meter²) on random-bred, male albino mice pretreated with γ -radiation (⁶⁰Co; 0.36 r/week; group I), UV (total 52.5 watt/min./meter²; group II), γ + UV (as above; group III), and on control mice were determined. After 24 hours, initial erythema progressed to burns, epithelial hyperplasia and dermatosis; 4-6 mo. after UV, 70/147 mice developed skin neoplasms (mainly of the ear, also the tail, spine and snout), accompanied by massive ulceration. Epithelial neoplasms (benign and malignant papillomas, keratoacanthomas and carcinomas) and sarcomas (rhabdomyosarcomas, chondrosarcomas) developed in 3/10 and 7/10 control mice, resp. Results for groups I, II and III, resp., were 5/24 and 19/24, 8/23 and 15/23, and 7/13 and 16/13 for epithelial neoplasms and

sarcomas, resp. Chronic γ -radiation decreased the animals' resistance toward carcinogenic effects of UV, and increased frequency and rate of appearance of malignant skin neoplasms. Preliminary irradiation with UV or UV + γ -radiation in small doses did not increase frequency of tumors, but did reduce the latent period for tumor development.

70-1745 SARCOMA INDUCED BY RADIOTHERAPY.

REPORT OF TWO CASES. (Rum.) Iancu, I. (Jassy Radiol. Clin., Rumania), G. Dobrescu, D. Timofte and C. Clement. Oncol. Radiol. 8(5):443-446, 1970.

A 59-yr.-old man with a varicose ulcer of 23 yr. duration, which showed signs of malignant transformation to a spinocellular carcinoma, was treated with external radiotherapy (RT) to both the ulcer (3600 r) and to a region of inguinal lymphadenopathy (2000 r). Some healing was seen and the ulcer region was removed surgically. The inguinal lymphadenopathy recurred 3 yr. after RT; the biopsy diagnosis was reticulum cell sarcoma. A 49-yr.-old woman with carcinoma of the cervix was treated for 2 yr. with RT (total 15,800 r). A varicose ulcer developed 4 yr. after the beginning of RT. Inguinal lymphadenopathy developed 15 yr. after the beginning of RT, and was treated with local RT (2400 r). The irradiated region became sclerotic and telangiectatic; it was excised several mo. later and identified as a reticulum cell sarcoma. It is concluded that the formation of radiation-induced sarcomas is independent of the nature of the ionizing radiation. Minimal tumor-inducing radiation doses have been described as 200-3000 r and the minimal latent period as 3 yr. in published reports.

70-1746 THE INFLUENCE OF IRRADIATION ON THE FREQUENCY AND RATE OF APPEARANCE OF BREAST TUMOURS IN RATS. (Rus.)

Moskalev, Iu. I., I. K. Petrovich and V. N. Strel'tsova. Biull. Eksp. Biol. Med. 34(4):95-99, 1969.

Frequency and rate of development of mammary tumors in random-bred, adult female rats was about the same after single doses of X- or γ -radiation (100, 300 or 600 r). Treatment (100 and 300 r) in prolonged or fractional doses had no effect on survival time or blood composition; in contrast, although many animals died of acute radiation sickness, prolonged and fractional admin. (600 r) significantly increased survival time. Hematological studies showed that single radiation induced more leukopenia than fractional treatment, but recovery from single doses was faster (14-21 days).

70-1747 INCREASED MALIGNANCY OF GLIOMAS INDUCED BY THERAPEUTIC MEASURES. (Ger.)

Müller, H.-A. (U. Würzburg Path. Inst., Germany). Verh. Deutsch. Ges. Path. 53:544-547, 1969.

severe metastasizing was observed in 3 pts. (1 male and 2 females, 12, 18 and 19 yr. old) after incomplete removal of malignant transformed or anaplastic astrocytoma followed by intensive Co-radiation therapy (to 7200 r) and admin. of cyclophosphamide (to 4.1 g). The pts. survived 13-263 days after brain surgery. Examination of tumor tissue at autopsy revealed greater cell density, increased number of voluminous multinucleated giant cells and appearance of undifferentiated cells. These cells are possibly of a previously undetected cell population resistant to therapy, or they represent new cells, adapted to therapeutic measures, which became malignant.

1748 FLUOROSCOPIC RADIATION AND RISK OF PRIMARY LUNG CANCER FOLLOWING PNEUMOTHORAX THERAPY OF TUBERCULOSIS. (E.) Gofman, J. W. (U. California Lawrence Radiat. Lab., Livermore) and A. R. Tamplin. Nature (London) 27(5255):295-296, 1970.

In a comparison of published data on radiation therapy of tuberculosis pts. in Nova Scotia and the incidence of lung cancer in pts. in Israel, a calculated 7.2-fold increase in expected risk due to fluoroscopy is found to be consistent with an observed 5-10-fold high risk of lung cancer in tuberculosis cases. Pneumothorax collapse therapy is implicated, rather than cigarette smoking, in the development of lung cancer in tuberculosis pts. Further studies with data from hospital records and follow-up studies of tuberculosis and lung cancer pts. as they relate to smoking, fluoroscopic radiation or chemical agents (i.e., isoniazid) are suggested.

1749 INFLUENCE OF ALTITUDE ON LATE EFFECTS OF RADIATION IN RF/Un MICE: OBSERVATIONS ON SURVIVAL TIME, BLOOD CHANGES, BODY WEIGHT, AND INCIDENCE OF NEOPLASMS. (E.) Mori-Chavez, J. (Cayetano Heredia Peruvian U. High Altitude Res. Inst., Lima), A. C. Upton, M. Salazar J. and J. W. Conklin. Cancer Res. 30(4):913-928, 1970.

Female, 10-week-old RF mice were sham-irradiated (controls) or admin. X-irradiation (150 or 300 r, to the whole body) and maintained throughout life either at sea level or high altitude (14,900 feet). Generally, the frequency of neoplasms was increased by radiation and reduced by high altitude. All types of lymphomas and leukemias occurred less frequently at high altitude than at sea level. Frequency of thymic lymphomas and granulocytic leukemias increased with irradiation. Frequency of lung tumors decreased with irradiation at sea level, but increased with or without irradiation at high altitude. Lung carcinomas were more common at high altitude than at sea level. Frequency of ovarian tumors was greater after irradiation, but unaffected by altitude. Miscellaneous neoplasms of various types and

sites occurred sporadically in all experimental groups, the total number was larger at sea level (15 cases) than at high altitude (5 cases). It is concluded that some long-term effects of irradiation may be markedly modified by subsequent exposure to high altitude, but that not all effects are similarly influenced.

70-1750 ACTION OF A FARADIC CURRENT ON THE DEVELOPMENT OF TRANSPLANTED WALKER 256 CARCINOSARCOMA AND ON CATECHOLAMINES OF THE TUMOR TISSUE. (Rum.) Milcu, St.-M. (Rumanian Inst. Endocr., Bucharest), H. Zimeï, V. Chivu and A. Măcrineanu. Stud. Cercet. Endocr. 20(5):445-449, 1969.

Male white rats were exposed to a faradic current (daily x 3 weeks) 24 hours after s.c. transplantation of Walker 256 carcinosarcoma. Changes in body and tumor wt. were determined and tumors were analyzed for catecholamines. Treated rats gained less wt. than controls, but their av. tumor wt. was 36% greater. The av. catecholamine content (noradrenalin was measured) was 0.4804 µg/g and 0.4090 µg/g for treated rats and controls, resp.

70-1751 STUDIES ON ONCOGENIC TRANSFORMATION, INDUCTION OF DNA SYNTHESIS AND T ANTIGEN FORMATION BY UV-IRRADIATED SIMIAN VIRUS SV40. (Ger.) Seemayer, N. (U. Freiburg Hyg. Inst., Germany), G. Seemayer and R. Haas. Z. Med. Mikrobiol. Immun. 155(2):123-132, 1969.

UV treatment (1-12 min.) strongly reduced infectivity, DNA synthesis and ability to produce T antigen of SV40 tested in monkey (*Cercopithecus aethiops*) kidney cell cultures, but caused only slight inhibition of oncogenic potency of the virus in vivo and in vitro. In vitro, only a minimal reduction of oncogenic transformation in hamster kidney cell cultures was observed. In vivo inj. of SV40 (0.1 ml suspension, s.c.) into groups of newborn golden Syrian hamsters resulted in the development of malignant transplantable tumors in 3/3, 1/4, 4/4, 2/3 and 6/12 animals (SV40 was previously irradiated for 1, 2, 4, 8 and 12 min., resp.) as compared to 5/6 inj. with non-irradiated virus. Tumor induction varied from about 4-5.5 mo. SV40-specific T antigen was seen in practically all nuclei of tumor cells and hamster kidney cells transformed in vitro. It is concluded that the ability to replicate, form T antigen and induce DNA synthesis is not a prerequisite for oncogenic potency of SV40 either in vivo or in vitro. Several interpretations of this phenomenon are presented and its possible significance for vaccine production is discussed.

70-1752 X-IRRADIATION OF BALB/3T3: SARCOMA-FORMING ABILITY AND VIRUS INDUCTION. (E.) Pollock, E. J. (Bureau Radiol. Health,

Rockville, Md.), S. A. Aaronson and G. J. Todaro. Int. J. Radiat. Biol. 17(1):97-100, 1970.

BALB/3T3 cells were grown in culture after X-irradiation (1500 rads); after 18-21 days colonies were selected and carried through 20-30 cell generations. Control colony-forming ability is generally about 30%; after irradiation it was 0.5%. After inoc. into weanling BALB/c mice, only one subclone produced tumors at the inoc. site in 17/20 (85%) animals after 10 weeks. Tumors were undifferentiated fibrosarcomas. Spleen cells from the mice contained complement-fixation antigen activity against murine leukemia group reactive antiserum; the cells, however, did not produce infectious virus in culture.

70-1753 RETENTION OF RADIOSTRONTIUM IN SOFT TISSUES. (E.) Brues, A. M. (Argonne Nat. Labs., Chicago, Ill.), H. Auerbach, D. D. Grube and G. M. DeRoche. Argonne Nat. Labs. Ann. Rep. ANL-7635:119-120, 1969.

For the soft body tissues, the plasma conc. curve is a satisfactory index of tissue conc. integrated through time. From these values, radiation dosage levels can be compared and evaluated. A sample of sperm from adult beagles showed little ^{85}Sr retention; total inj. of 7.4×10^7 counts/min. resulted in 2.8 counts/min. after washing. It is concluded that deposition of radiostrontium in sperm is not a significant fallout factor.

70-1754 LATE EFFECTS OF FAST NEUTRONS AND GAMMA-RAYS IN MICE AS INFLUENCED BY THE DOSE RATE OF IRRADIATION: INDUCTION OF NEOPLASIA. (E.) Upton, A. C. (State U. New York Health Sci. Ctr., Stony Brook), M. L. Randolph and J. W. Conklin. Radiat. Res. 41(3):467-491, 1970.

Virgin 8-10-week-old male and female RF/Un mice were given whole body irradiation at various schedules and rates. The frequency of neoplasms was max. for an intermediate dose (approximately 300 rads) after acute irradiation, but a comparative increase was noted after treatment with neutrons and a comparative decrease was seen after γ -ray treatment. The oncogenic effects of irradiation did not completely account for its life-shortening effects. The dose-effect relationship of radiation with various neoplasms was presented, including myeloid leukemia, thymic lymphoma, other lymphomas, ovarian tumors, pulmonary adenoma and solid neoplasms of other organs.

70-1755 A SEARCH FOR LATE RADIATION EFFECTS AMONG MEN WHO SERVED AS X-RAY TECHNOLOGISTS IN THE U.S. ARMY DURING WORLD WAR II. (E.) Miller, R. W. (NCI, Bethesda, Md.) and S. Jablon. Radiology 96(2):269-274, 1970.

A follow-up study was made as to the cause of death among 6,560 male Caucasians trained as X-ray technicians during World War II, using 5,304 medical laboratory technicians and 1,522 pharmacy technicians as controls. The only significant values were an elevated frequency of lymphoma among pharmacy technicians (5 observed, as opposed to 1.8 expected) and 17 X-ray technicians died of respiratory cancer compared to 4 controls; the latter difference was due, in part, to a deficit among the controls. No radiation effect was observed on the frequency of leukemia or the sex ratio of the subjects' children.

70-1756 STUDIES ON THE BONE MARROW OF A-BOMB EXPOSED IN HIROSHIMA BY AUTORADIOGRAPHY. (E.) Araki, F. (Yamaguchi U. Sch. Med., Ube, Japan) and Y. Sugihara. Hiroshima J. Med. Sci. 18(4):247-252, 1969.

Autopsy specimens of bone marrow from 19 (7 subacute, 8 subchronic, 4 chronic) A-bomb exposed persons (age ranging from a premature infant to 60 tr.) in Hiroshima were examined autoradiographically to determine if radioactivity was still present after 20 yr. Bone marrow aplasia was seen in 5/7 and slight regeneration was seen in 2/7 subacute cases. Regenerative changes occurred in 6/8 subchronic cases; 1/8 had aplasia with reticulum cell proliferation and 1/8 was normoplastic. All 4 chronic cases showed only slight regenerative changes, with nearly-normal bone marrow. Radioactivity was found in the bone marrow of 6/19 cases (2/7 subacute, 3/8 subchronic, 1/4 chronic); 5/6 were under 24 yr. of age. Tissue from the premature infant demonstrated radioactivity, indicating transfer into the fetus through the placenta.

70-1757 CHROMOSOME ABERRATIONS AND MALIGNANT DISEASE AMONG A-BOMB SURVIVORS. (E.) Bloom, A. D. (U. Michigan Med. Sch., Ann Arbor), Y. Nakagome, A. A. Awa and S. Neriishi. Amer. J. Public Health 60(4):641-644, 1970.

Studies of atomic bomb survivors in Japan revealed that 35-62% of those exposed to over 100 rads have residual chromosomal aberrations. These abnormal chromosomes, which are dose- and age-dependent, can produce subpopulations, although not necessarily malignant, *in vivo* which are potentially related to neoplasia. The possibility of fibroblast transformation occurring in conjunction with chromosome breakage is suggested, but it is concluded that factors such as karyotypic abnormalities would be difficult to apply to large populations in an attempt to detect a premalignant state.

70-1758 INDUCTION OF SOLID TUMORS BY PERINATAL IRRADIATION OF MICE. (E.) Gates, O. (New England Deaconess Hosp. Cancer Res. Inst., Boston, Mass.) and S. Warren. Fed Proc. 29(2): 818, 1970.

See also abstract nos: 1711, 1716, 1717, 1727, 1804, 1841, 1911, 1926, 2010, 2014, 2018, 2095

70-1759 AUTOMATIC DATA PROCESSING TECHNIQUES FOR CARCINOGENESIS STUDIES. (E.)

Greenblatt, M. (U. Nebraska Med. Ctr. Eppley Inst., Omaha), R. Montesano, L. Wombolt and P. Hubik. J. Nat. Cancer Inst. 44(5):1037-1045, 1970.

Methods of automatic data processing, adapted to the evaluation of results of chronic studies of chemical carcinogens in animals, are described. Several methods of standardized reporting of data are suggested.

70-1760 GENE ELIMINATION IN CARCINOGENESIS: REINTERPRETATION OF THE SOMATIC

MUTATION THEORY. (E.) Fahmy, O. G. (Chester Wadsworth Res. Inst. Cancer, London) and M. J. Fahmy. Cancer Res. 30(1):195-205, 1970.

Various carcinogens were tested in Drosophila melanogaster for the induction of point mutations, small chromosome deletions resulting in Minutes, and major chromosomal rearrangements. Point mutations were produced by alkylating agents and nitroso compounds according to dose and structure. Urethan and its derivatives had weak mutagenic activity on mature sperm, while all polycyclic hydrocarbons and aromatic amines tested were inactive. There was no significant correlation between mutagenicity and carcinogenicity. All agents induced Minutes, which seemed to have some correlation with carcinogenicity, and which were caused in part by interference with reproduction or repair of genetic DNA. Only the di- and polyfunctional alkylating agents caused visible chromosomal changes, the other compounds being ineffective.

70-1761 A CELL CULTURE SYSTEM FOR THE ASSESSMENT OF TUMOR-PROMOTING ACTIVITY.

(E.) Sivak, A. (New York U. Med. Ctr. Inst. Environ. Med., N. Y.) and B. L. Van Duuren. J. Nat. Cancer Inst. 44(5):1091-1097, 1970.

The cell culture system described provides a rapid and reproducible system for examining a variety of compounds suspected of having tumor-promoting activity at different dose levels. In a mixed culture system containing an excess of contact-inhibited cells, the growth of viral or chemically transformed cells was enhanced by tumor-promoting agents from tobacco leaf extracts, by phorbol esters from croton oil and by other chemicals. When toxicity was at a minimum this enhancement was directly related to dose and to density of contact-inhibited cell overlay. These results are comparable to those found for mouse skin.

70-1762 BRONCHOPULMONARY CANCER AFTER ASBESTOSIS. (Fr.) Desbordes, J. (Med. Ctr.,

Le Havre, France), F. Manouvrier, J. Tayot, J.-L. Ernoult, M. Boisseau, G. Dousset and A. Dauty. J. Franc. Med. Chir. Thorac. 27(7): 809-821, 1968.

A woman who had been an asbestos worker for 13 yr. (from age 22-35), and did not smoke, developed epidermoid bronchial carcinoma which metastasized. Autopsy revealed many asbestos bodies (previously found in the sputum) in the intra-alveolar fibers of the lungs. Systematic bronchial endoscopy is recommended for all cases with asbestos exposure of more than 20 yr.

70-1763 ASBESTOSIS AND NEOPLASTIC DISORDERS OF THE HEMATOPOIETIC SYSTEM. (E.)

Gerber, M. A. (1249 Park Ave., New York, N. Y.). Amer. J. Clin. Path. 53(2):204-208, 1970.

An 11-yr. study of 1334 autopsies of pts. age 50 yr. or over performed from 1958-1969 at Middlesex General Hospital revealed 37 cases with hematopoietic tumors (2.8%) as compared to 35 cases of asbestosis (2.6%). Association of 5 cases (3/5 with occupational exposure) of asbestosis with hematopoietic tumors gave a significantly higher frequency of 14.3%, as compared to an overall frequency of 2.8% for such tumors.

70-1764 THE ROLE OF TRACE METALS IN CHEMICAL CARCINOGENESIS: ASBESTOS CANCERS.

(E.) Dixon, J. R. (Consumer Protection Environ. Health Serv., Cincinnati, Ohio), D. B. Lowe, D. E. Richards, L. J. Cralley and H. E. Stokinger. Cancer Res. 30(4):1068-1074, 1970.

Results of an in vitro study of the effects of chrysotile asbestos and trace amounts of metals on the benzpyrene (BP) hydroxylase system in the microsomal fraction of homogenates of rat lungs showed that this enzyme system could be activated or inhibited, depending upon the relative conc. of the metal added. While Cu^{2+} , Mg^{2+} , Fe^{2+} , Zn^{2+} , Ni^{2+} and Co^{2+} significantly stimulated the BP hydroxylase enzyme at low conc. and inhibited it at higher conc., Be^{2+} , Fe^{3+} and Cr^{6+} significantly inhibited the enzyme. As^{3+} , Se^{4+} and Cr^{3+} had no effect. When trace metals were extracted from chrysotile asbestos and added to enzyme reaction mixtures, enzyme activity was inhibited by about 73%. This suggests that chrysotile has the potential of interfering with BP detoxication and could therefore contribute to carcinogenesis. BP hydroxylase activity in human lungs could be stimulated by addition of Cu^{2+} (3 μg) and inhibited by addition of Ni^{2+} (6 μg); these results were similar to findings for rat lungs. These results support the hypothesis that in the induction of asbestos cancer, trace metals have an active role, asbestos has a passive role

as a metal carrier and BP (or related polycyclic aromatic hydrocarbons) derived from the environment has a critical mediating role. The major determinant for carcinogenesis is the residence time of unmetabolized BP in the lung. With unmetabolized BP as the carcinogen, any action (such as trace-metal inactivation) that slows metabolism increases residence time and the carcinogenic risk.

70-1765 IDENTIFICATION OF Cannabis CONSTITUENTS IN THE PARTICULATE MATTER OF SMOKE.

(E.) Fish, F. (U. Strathclyde, Glasgow, Scotland) and W. D. C. Wilson. J. Forensic Sci. Soc. 91(1-2):37-40, 1969.

Smoke from cigarettes composed of Cannabis resin (50-60 mg) or flowering tops (400-450 mg) and commercial tobacco, to give a total wt. of 1 g, was dispelled into the atmosphere by a smoking machine, and particulate matter subsequently collected by drawing air through a glass filter for 5 or 10 min. The concentrate prepared from the filter was analyzed by thin-layer, gas-liquid and gas chromatography and the presence of cannabidiol, tetrahydrocannabinol and cannabinol was confirmed by all chromatographic methods for samples which were previously shown to contain these compounds.

70-1766 THE DETECTION OF Cannabis CONSTITUENTS IN THE MOUTH AND ON THE FINGERS OF SMOKERS.

(E.) Stone, H. M. (Sci. Indust. Res. Dept., Private Bag, Petone, Wellington, New Zealand) and H. M. Stevens. J. Forensic Sci. Soc. 91(1-2):31-34, 1969.

Cannabinol condensates were detected up to 3 hours after smoking in a chloroform wash of the thumb and first 2 fingers by elution on a silica gel plate and examination under UV light. Confirmation was obtained by gas chromatography or use of an alumina plate. This method could determine which hand held the reefer or handled the resin, and could differentiate between Cannabis and tobacco smokers. A similar method detected cannabinol in an ethanol and saline mouthwash 0.5-1 hour after smoking.

70-1767 CANCER AND EXPOSURE TO MINERAL OILS.

(E.) Parkes, H. G. (Industr. Med. Surg., PO Box 546, Miami, Fla.). Industr. Med. Surg. 39(2):78-81, 1970.

A report on a legal ruling concerning the death of a man with cancer of the scrotum who had been exposed to mineral oils in his occupation as a tool setter is mentioned in support of the value of examination and preventive measures for all people exposed to mineral oils in their work. The use of solvent-refined oils in the rubber

industry, as well as education on health and hygiene precautions, is suggested.

70-1768 LUNG CANCER IN RATS CAUSED BY INTRA-TRACHEAL ADMINISTRATION OF SMOKE PRODUCTS. (Rus.) Borisiuk, Iu. P. (Kiev Sci. Res. Inst. Exp. Clin. Oncol., USSR). Vop. Onkol. 15(6):49-53, 1969.

Cross-bred, 2.5-3.0-mo.-old Wistar rats were treated by intratracheal intubation of cigarette tar (CT; 3,4-benzpyrene (BP) content = 0.6 µg/g; dose of 40-50 mg x 10, 1 mo. intervals between intubations), denicotinized tar (DT) or CT neutral fraction (NF; BP content = 1.5 µg/g; dose of 50 mg/intubation) and their respiratory organs were studied; rats treated by protein blood substitute (BK-8) served as controls. The number of animals which survived to the end of the experiment, duration of intubation (in mo.), survival time after intubation (in mo.) and number of rats with pulmonary changes were: for the CT group (total 200), 24, 10, 8 and 0, resp.; for the DT group (45), 9, 8, 12 and 1 (metaplasia with signs of infiltrative growth), resp.; and for the NF group (100), 14, 8, 12 and 3 (2/3 keratosis squamous cell carcinoma, 1/3 papillary proliferation of bronchial epithelium), resp. Histological study after 1 mo. of treatment showed acute and subacute inflammatory changes in lungs which became chronic in character, accompanied by development of granular, filamentous and fibrous connective tissue. In bronchial mucosa, partial death and desquamation occurred, followed by replacement with granular tissue or immature, poorly-differentiated epithelium.

70-1769 PRECIPITATION REACTION BETWEEN CERTAIN HUMAN SERA AND SOLUBLE EXTRACTS OF TOBACCO. (Fr.) Kreis, B. (Cochin Hosp., Paris), A. Peltier, S. Fournaud and S. Dupin-Girod. Ann. Med. Intern. 121(4):437-440, 1970.

Aqueous extracts of commercial tobacco produced a precipitation reaction in 407/651 (62.5%) different human sera. The strength of reaction varied according to type of tobacco, being less for the lighter-colored types. Frequency of reaction varied according to type of respiratory disorder (72% for pulmonary cancer, 50% for pulmonary insufficiency), number of cigarettes smoked per day (ranged from 43.5% for 0 cigarettes to 62% for more than 20), and age (57% at 3 mo., decreasing to 17% at 16 mo. and then increasing to 63% over 16 yr.). It is suggested that the precipitation is due to an antigen in tobacco extract and that a non-specific antigen-antibody (tobacco-IgG) reaction occurs; cross-reactions may also be involved. The pathogenic significance of some precipitation reactions (for those of tobacco as well as various vegetable extracts such as tea and coffee) is also discussed.

10-1770 NO DEMONSTRABLE LONG TERM EFFECTS OF CIGARETTE SMOKING ON THE MUCOCILIARY MECHANISM OF THE HUMAN LUNG. (E.) Pavia, D. (TUC Centenary Inst. Occupat. Health London Sch. Hyg. Trop. Med.), M. D. Short and M. L. Thomson. *Nature (London)* 226(5252):1228-1231, 1970.

In a study of the long-term effects of smoking in the lung, 39 subjects (10/22 male smokers and 17 female smokers) had smoked an av. of 54.4 yr. and 46.8 yr., resp. Aerosol exposure to ^{99}Tc -labeled polystyrene particles (5 μm , total 10 ml vol. inspired) and subsequent expectoration were analyzed statistically. No difference due to impairment of mucociliary efficiency between smokers, nonsmokers, ex-smokers and abnormal lung disease) subjects was found.

10-1771 DETECTION OF POTENTIAL WEAK CARCINOGENS AND PROCARCINOGENS. II. CARCINOGENICITY OF TERTIARY BUTYL HYDROPEROXIDE. (E.) Oshino, H. (Nat. Cancer Ctr. Res. Inst., Hiroshima, Tokyo), G. Chihara and F. Fukuoka. *Cancer Res.* 30(12):121-124, 1970.

The summation of a weak carcinogenic effect of tert-butyl hydroperoxide (tBHP) or tert-butanol (tBUT) with that of a submanifestational dose of potentially carcinogenic 4-nitroquinoline 1-oxide (NQO) is studied. Twenty applications of QO (0.05 mg) or 270 applications of tBHP (16.6% conc.) failed to produce tumors. Combined treatment consisting of 20 applications of NQO followed by either 270 applications of tBHP or tBUT resulted in 9 and 1 tumors, resp. (a statistically significant difference). The possibility is suggested that peroxide compounds or oxygen-containing free radicals play a role in the chemical carcinogenesis of some classes of chemicals.

10-1772 CARCINOGENIC ACTION OF THE INTERMEDIATES OF FLUORESCENT WHITENING AGENTS, 5-NITROACENAPHTHENE AND 5-AMINOACENAPHTHENE. (Jap.) Hashida, C. (Jikei U. Sch. Med., Tokyo). *J. Hyg.* 24(2):263-269, 1969.

Grouping of 20 mice with 5-nitroacenaphthene (NA; 0.05% soln., 2 admin./week x 18 mo., i.p.) and 20 mice with 5-aminoacenaphthene (AA; same dosage) was followed by study of all animals surviving more than 6 mo. Of the animals receiving NA, 11/11 had leukemia, 2/11 had reticulum cell sarcoma and 1/11 developed mammary carcinoma. Of the AA-treated animals, 3/15 had leukemia and 1/15 developed lymphosarcoma. Tumor incidence was 42% for both groups. Cellular infiltration was noted in all cases. Wax pellets containing 10% NA and AA were implanted in the urinary bladders of mice. Of the NA-treated animals, 15/50 developed carcinomas as did 12/49 AA-treated animals, with a rate 14% and 25%, resp., compared to 9% for controls. The urine from dogs fed AA in the diet (100 mg/kg/week) was examined by

thin-layer chromatography. AA was excreted as the glucuronide of an amine; the carcinogenic property of the amine was not determined.

70-1773 DETERMINATION OF NITRATE REDUCTION BY BACTERIA OF THE ENTEROBACTERIACEAE FAMILY FROM THE STANDPOINT OF CARCINOGENICITY OF THE REAGENTS. (Ger.) Parráková, E. (Res. Inst. Hyg., Bratislava, Czechoslovakia), J. Mayer and J. Janoušková. *Arch. Hyg. Bakt.* 153(3):230-233, 1969.

The reduction of nitrate to nitrite by enterobacteriaceae is usually determined by the Griess-Ilosvay method which uses strongly carcinogenic α -naphthylamine as a reagent. Since this compound in either the powdered form or in aqueous solution (as used in the laboratory) is detrimental to health, a new method which uses a noncarcinogenic sulfur derivative (1-naphthylamine-7-sulfonic acid) was developed. Comparative studies with different strains of bacteria showed the new method to be superior to the Griess-Ilosvay method.

70-1774 CYCASIN-INDUCED RENAL TUMOURS IN THE WISTAR RAT, WITH SPECIAL CONSIDERATION OF ADENOMAS. (Ger.) Gusek, W. (U. Hamburg Path. Inst., Germany) and W. Mestwerdt. *Beitr. Path. Anat.* 139(2):199-218, 1969.

When 28-day-old Wistar rats were fed cycasin (a glycoside derived from the nut of *Cycas circinalis*; 50 mg/100 g feed x 21 days), 24/170 died of cytotoxic effects before the end of the treatment period; an additional 50/170 died by the end of the minimal latency period for tumor induction. Renal tumors in 89/96 survivors totaled 244, including interstitial, mixed mesenchymal and Wilms' tumors, adenomas, cavernomas, dysplasias, and 1 myosarcoma. Adenomas (39/244) were small and usually demonstrable only by histologic study; they included basophilic, eosinophilic and oncocytic cell types. Some were solid and others were cysto- or tubulopapillary. As compared to normal renal parenchymal tissue, acid phosphatase activity in adenomatous tissue was essentially unchanged; lactate dehydrogenase activity varied from comparable to slightly reduced; leucine aminopeptidase and glucose-6-phosphate dehydrogenase activities were uniformly somewhat reduced; succinate dehydrogenase activity was markedly diminished; alkaline phosphatase, nonspecific esterase and carboanhydrase activities were lacking. However, alkaline phosphatase activity was markedly increased in adenomatous stroma.

70-1775 PREFERENTIAL LOCALIZATION OF GALLIUM-67 CITRATE IN TISSUES OF LEUKEMIC MICE. (E.) Swartzendruber, D. C. (Oak Ridge Assoc. Univ., Tennessee), B. L. Byrd, R. L. Hayes, B. Nelson and R. L. Tyndall. *J. Nat. Cancer Inst.* 44(3):695-700, 1970.

Normal male and female AKR/J mice (7 and 13 weeks old) were inj. with ^{67}Ga citrate (7 mg/kg; 2 $\mu\text{C}/\text{animal}$, i.v.) and the age-dependency of ^{67}Ga uptake in the thymus determined. Less ^{67}Ga was deposited in the thymus, spleen and bone of the older mice than in the 7-week-old animals (2.05 g and 6.56 g, resp.). In 8-10-mo.-old male and female AKR/J mice, classified as leukemic or nonleukemic and inj. with ^{67}Ga , the conc. in the thymus of leukemic mice was 8-fold that for nonleukemic mice, which was about the same as for the 13-week-old leukemic animals. Conc. of ^{67}Ga in the kidneys of older nonleukemic mice was, unexpectedly, double that in young mice or older leukemic mice; also, ^{67}Ga conc. in the spleen was not increased in leukemic mice. Comparison of ^{67}Ga conc. in male and female, 7-8-week-old BALB/c mice inoc. with Rauscher leukemia virus (RLV; 10,000 LD₅₀, i.p.) and matched controls showed increases in blood (4-fold), spleen, liver and lungs (all 2-fold) of the RLV-treated mice. The possibility of early recognition of leukemogenesis by altered ^{67}Ga localization patterns is suggested.

70-1776 ASTHMA, ARSENIC, AND CANCER. (E.)

Novey, H. S. (U. California Sch., Med., Los Angeles) and S. H. Martel. J. Allerg. 44(5):315-319, 1969.

A case report is presented of a 56-yr.-old woman with a Bowen's type carcinoma of the skin and an 8 yr. history of skin lesions, including keratoses, hyperpigmentation and carcinoma. She had been taking one teaspoonful of a preparation known as B & M daily for 30 yrs. for bronchial asthma. The preparation contained Fowler's solution (8-10 ml), potassium iodide (16-20 ml), spirits of ammonia (16-20 ml), syrup of sassafras compound (2 ounces) and water to 240 ml; an estimated 21 g of arsenic trioxide had been consumed by the pt. over the 30-yr. period.

70-1777 TWO SPECIFIC AZODYE-CARCINOGEN-BINDING PROTEINS OF THE RAT LIVER. THE IDENTITY OF AMINO ACID RESIDUES WHICH BIND THE AZODYE. (E.) Ketterer, B. (Middlesex Hosp. Med. Sch. Courtauld Inst. Biochem., London) and L. Christodoulides. Chem. Biol. Interactions 1(2): 173-183, 1969/70.

Male Wistar rats (200 g) were inj. with 3'-methyl-4-dimethylaminoazobenzene (MeDAB; 50 mg in corn oil, i.p.) and ^{35}S -labeled amino acid (60 μC in saline, i.p.). The basic and low molecular wt. proteins (molecular wt. 45,000 and 13,800, resp.) from livers were purified and studied for MeDAB binding. A "fingerprinting" method was used to manipulate the small amounts of bound components after pronase digestion and alkali-ethanol reflux. MeDAB-bound components from both proteins were radioactive after admin. of ^{35}S -L-methionine, whereas MeDAB-bound components from the basic protein, only, were radioactive after ^{35}S -L-cysteine admin. It is concluded that MeDAB metabolites

bind to cysteine residues in the basic protein, whereas MeDAB binds to methionine residues in the small molecular wt. protein.

70-1778 BLASTOMOGENIC PROPERTIES OF SOME DERIVATIVES OF DITHIOCARBAMIC ACID (HERBICIDES ZINEB AND ZIRAM). (Rus.) Chernov, O. V. (All-Union Sci. Res. Inst. Hyg. Toxicol. Pesticides, Leningrad, USSR) and I. I. Khitsenko. Vop. Onkol. 15(4):71-74, 1969.

Admin. of the fungicide zinc ethylene-bis (dithiocarbamate) (Zineb; 3,500 mg/kg/week, 6 admin., p.o.) or urethan (U; 500 mg/kg) gave the following results after 3 mo.: in strain A and C57BL mice, resp., adenomas developed in 35/101 (34.6%) and 6/79 (7.6%), as compared to 30/97 (30.9%) and 0/87 untreated controls; all and 11/50 (22%) of the U-treated mice developed multiple lung adenomas. When Zineb was admin. to C57BL mice (1,750 mg/kg/week, 11 admin., p.o.), after 6 mo., 2/29 mice (6.9%) had adenomas as compared to 0/59 controls, while 3/17 (17.7%) U-treated mice had adenomas. Strain A and C57BL mice were also admin. the fungicide zinc dimethyldithiocarbamate (Ziram; 75 mg/kg/week, 20 admin., p.o.) or U. After 6 mo., 42/82 (51.2%) and 4/54 (7.4%) showed lung adenomas as compared to 23/54 (42.6%) and 0/28 controls, for the A and C57BL strains, resp.; all the U-treated mice had tumors. Ziram lowered oxido-reductase activity the first 2 weeks; then it increased, particularly in the adenomas. Zineb produced immediate increase in activity of oxido-reductases, as well as glucose-6-phosphate dehydrogenase and lactate dehydrogenase. Liver cells showed fatty dystrophy of the cytoplasm, with gradual increase in RNA content in the 6 mo. period. U induced almost the same changes as produced by Zineb.

70-1779 CARCINOGENICITY TESTING OF SELECTED FOOD ADDITIVES BY PARENTERAL ADMINISTRATION TO INFANT SWISS MICE. (E.) Epstein, S. S. (Child. Cancer Res. Found. Inc., Boston, Mass.), K. Fujii, J. Andrea and N. Mantel. Toxicol. Appl. Pharmacol. 16(2):321-334, 1970.

Swiss albino mice were admin. 6 food additives [safole, alginic acid, polyoxyethylene-(20)-sorbitan monostearate (Tween 60), 1,3,5-trimethyl-2,4,6-tris-(3,5-di-*tert*-butyl-4-hydroxybenzyl)benzene (Ionox 330), 6-ethoxy-2,2,4-trimethyl-1,2-dihydroquinoline (Santoquin) and 2,4-bis(4-hydroxy-3,5-di-*tert*-butylphenoxy)-6-(*n*-octylthio)-1,3,5-triazine (RA-858); s.c. on days 1, 7, 14 and 21 of life] in a test for toxicity and carcinogenicity. Frequency of hepatomas was 58% in mice admin. safole (total dose 6.6 mg), as compared to 5% in controls. Treatment with Ionox 330 produced no significant change in frequency of hepatomas. No hepatomas developed in either females or males of the other treatment groups. Large lung adenocarcinomas developed in 5/43 safole-treated

males, 1/38 safrole-treated females, 1/25 males treated with Tween 60 and in no other treatment groups. Frequency of lung adenomas was not significant. A slight increase in development of lymphomas was seen for males and females of all treatment groups (except RA-858) at various dosages.

70-1780 PRODUCTION OF URINARY BLADDER CARCINOMAS IN MICE BY SODIUM SACCHARIN. (E.)

Bryan, G. T. (U. Wisconsin Med. Sch., Madison), E. Ertürk and O. Yoshida. Science 168(3936): 1238-1240, 1970.

Pellets of sodium saccharin (NaS; 20%) and cholesterol (pellet wt.=20-24 mg) were implanted in the bladder lumens of 60-90-day-old female Swiss mice and their rate of disappearance measured. The bladder lumens of groups of 100 mice were implanted with either pure cholesterol or NaS + cholesterol (1:4) and bladder carcinomas of animals surviving more than 175 days examined and classified according to infiltration. By 5.5 hours, 50% of the saccharin in the bladder disappeared and 99% was eluted from the pellets by 1.5 days. Frequency of bladder carcinomas was 47% and 52% for NaS-treated mice in comparison to 13% and 12% for controls (cholesterol alone). Tumors were often multiple with high mitotic activity and pleomorphism. Other tissues of the mice responded to the NaS as did controls. Mouse bladder response to NaS is considered more severe than it is to sodium cyclamate.

70-1781 ASSAY OF FRACTIONS OF BRACKEN FERN (*Pteris aquilina*) FOR CARCINOGENIC ACTIVITY. (E.) Pamukcu, A. M. (U. Ankara Coll. Vet. Med., Turkey), J. M. Price and G. T. Bryan. Cancer Res. 30(4):902-905, 1970.

Fractions were obtained from fresh bracken fern (*Pteris aquilina*) by extraction with cold and hot methanol, followed by ethyl ether. Pellets containing residues of these fractions were implanted into bladder lumens of female Swiss albino mice, while controls received only pure cholesterol pellet implants. The frequency of bladder carcinomas in mice treated with residues of the various fractions was 8/15 (53%), 5/20 (25%), 1/11 (9%), 7/18 (39%), 10/18 (56%) and 5/19 (26%). The frequency of papillomas in mice ranged from 9-42%. There was no indication of metastasis during the 55 weeks of the experiment. These findings suggest that one or more carcinogenic substances, soluble in methanol but of unknown nature, occur in the bracken fern itself. A relationship between the use of bracken fern as food in the U.S., New Zealand, and in Japan (a country with a high incidence of stomach cancer) and its carcinogenic activity is suggested.

70-1782 CANCER OF THE URINARY BLADDER AS A LATE EFFECT OF EXPOSURE TO CHEMICAL

WAR MATERIALS (POISON GAS). (Ger.) Lindenfelser, R. (Rhine-Westphalian Tech. Inst., Aachen, Germany). Z. Urol. 63(3):175-177, 1970.

A case of a 68-yr.-old man who developed a predominantly papillary carcinoma of the urinary bladder 20 yr. after a 17-mo. occupational exposure to chemical warfare agents (such as mustard gas and phosgene) in a military research institution is described.

70-1783 THE POSSIBLE ROLE OF HYDROPHOBIC INTERACTIONS OF POLYCYCLIC AROMATIC HYDROCARBONS WITH PROTEIN IN CHEMICAL CARCINOGENESIS. (E.) Franke, R. (Tech. Univ., Dresden, Germany). Molec. Pharmacol. 5(6):640-657, 1969.

The interrelationship of 34 polycyclic aromatic hydrocarbons and their carcinogenic activity, chemical reactivity and hydrophobic interactions with protein were investigated using methods of partial and multiple correlation and regression analysis. Hydrophobic interaction was found to be necessary for chemical carcinogenesis, possibly due to the induction of a conformational change in a receptor protein, but was of secondary importance compared to the chemical reactivity of the hydrocarbons. An index was presented which grouped hydrocarbons according to carcinogenic activity and described variations in activity due to polar or alkyl group substituents. The results were consistent with the K-L-region theory and the protein deletion hypothesis.

70-1784 INITIATING ACTIVITY OF AROMATIC HYDROCARBONS IN TWO-STAGE CARCINOGENESIS. (E.) Van Duuren, B. L. (New York U. Med. Ctr., Inst. Environ. Med., N. Y.), A. Sivak, B. M. Goldschmidt, C. Katz and S. Melchionne. J. Nat. Cancer Inst. 44(5):1167-1173, 1970.

Topical application of various aromatic hydrocarbons to the backs of female ICR/Ha Swiss mice was followed 2 weeks later by treatment with phorbol myristate acetate (PMA; 2.5 µg in 0.1 ml acetone, 3 applications/week x 58-60 weeks). From 51-74 days after primary treatment, dibenz(a,c)anthracene (1.0 mg/100 microliter benzene) and benz(a)anthracene (same dosage) induced tumors in 25/70 and 10/20 mice, resp. Perylene (0.8 mg/200 µliter benzene) and benzo(g,h,i)perylene (same dosage) did not significantly induce tumors; 7,12-dimethylbenzanthracene induced tumors in 19/20 mice. Tumors were predominantly papillomas and some squamous cell carcinomas. Single doses of the hydrocarbons alone failed to induce tumors. The relationship of these hydrocarbons to tobacco carcinogenesis, as well as to the tumor-promoting action of PMA with weak carcinogens in a 2-stage process, is emphasized.

70-1785 CARCINOGENIC SUBSTANCES IN WATER AND SOIL. XXVI. ROUTINE METHODS FOR THE DETERMINATION OF POLYCYCLIC AROMATIC COMPOUNDS

IN WATER. (Ger.) Borneff, J. (U. Mainz Inst. Hyg., Germany) and H. Kunte. Arch. Hyg. Bakt. 153(3):220-229, 1969.

A simple method for the determination of carcinogenic polycyclic aromatic compounds in samples of sewage-contaminated ground water, and to determine the efficiency of surface water purification, is described and the advantages are discussed. Amounts greater than about $50 \mu\text{g}/\text{m}^3$ in ground water and $100 \mu\text{g}/\text{m}^3$ in drinking water (these are standard levels) indicate a need to inspect the water treatment plant; values greater than $200 \mu\text{g}/\text{m}^3$ indicate the water should be rejected.

70-1786 DETERMINATION OF POLYNUCLEAR HYDROCARBONS IN ATMOSPHERIC DUST BY A COMBINATION OF THIN-LAYER AND GAS CHROMATOGRAPHY. (E.) Brocco, D. (U. Rome CNR Inst. Analyt. Chem.), V. Cantuti and G. P. Cartoni. J. Chromatogr. 49(1):66-69, 1970.

A method for analyzing atmospheric dust and its polynuclear hydrocarbons by combined thin-layer and gas chromatography is described. The combined method isolated and purified the sample rapidly and allowed for high sensitivity and resolution in evaluation of constituents.

70-1787 STUDY OF THE FATE OF BENZ- α -PYRENE IN THE SOIL. (Rus.) Shcherbak, N. P. (Inst. Exp. Clin. Oncol., Moscow). Vop. Onkol. 15(4):75-79, 1969.

Soil samples from 4 different areas (industrial, outside industrial, small village and forest) were analyzed for 3,4-benzpyrene (BP; in mg/kg of air-dried soil) content, resulting in the following values: 0.016-8.18, 0.007-5.51, 0.018-8.01 and 0.039-8.35 in spring, summer, fall and winter, resp. Filtration of BP from the surface into deeper layers was also observed. Plants (aster and nasturtium) cultivated in soil contaminated by BP (up to 7.0 mg/kg in the experimental group, 0.15 mg/kg for controls) showed accumulation of BP in the tissues. For all plants of the experimental group, BP was found in 0.39-0.59 mg/kg amounts, and was not detected in the controls. In extracts of the experimental and control plants, BP content was 0.057 and 0.009 mg/kg, resp. It is concluded that a decrease in BP content in the soil is due to 2 processes: its filtration into deeper layers and its absorption by plants; neither of these processes result in BP inactivation.

70-1788 EXPERIMENTAL STUDY OF THE EFFECTIVENESS OF REMOVAL OF CARCINOGENIC HYDROCARBONS DURING THE PURIFICATION AND DISINFECTION OF WATER. (Rus.) Il'nitskii, A. P. (Inst. Exp. Clin. Oncol., Moscow). Gig. Sanit. 34(9):26-29, 1969.

The effect of precipitation, flocculation, filtration and some methods of detoxification in the purification of water was determined by measurement of 3,4-benzpyrene (BP) content. In experiments with precipitation (method I), flocculation and precipitation (method II), filtration (method III) and flocculation and filtration (method IV), effectiveness was 57%, 90%, 99% and 99%, resp. Effectiveness of water purification was less with semi-industrial filtration processes than with experimental use of filtration columns. Methods I, II and IV were used to determine effectiveness of different stages of water purification, and method IV was found most effective (89%). Detoxification of water by chlorination decreased BP conc. after 30 min. by about 30%. Results were similar after UV-irradiation for 30 min.; after 60 min., detoxification was 20% more than for chlorination. Exposure to ozone for 5 min. decreased BP conc. 200-fold, and no unchanged BP was detected after 7.5 min.

70-1789 DETERMINATION OF 3,4-BENZPYRENE IN AIR. (Rus.) Nemenko, B. A. (Kazakh Sci. Res. Inst. Oncol. Radiol., Alma-Ata, USSR) and N. A. Mazina. Gig. Sanit. 34(5):91-92, 1969.

A method for the qualitative and quantitative determination of 3,4-benzpyrene (BP) content in the air is described. Analysis of 15 air samples from the city of Alma-Ata showed a BP content of 0.022-0.413 $\mu\text{g}/100 \text{ m}^3$ air. The greatest value was found for the main city street with intensive traffic.

70-1790 QUANTITATIVE DETERMINATION OF 3,4-BENZOPYRENE IN THE AIR NEAR GAS-WORKS RETORTS. (E.) Strömberg, L. E. (U. Stockholm Inst. Analyt. Chem.) and G. Widmark. J. Chromatogr. 49(2):334-340, 1970.

A method for statistical, quantitative analysis of the content of 3,4-benzpyrene and its derivatives in samples of air from the area of gas works retorts by thin-layer (using silica gel) and gas chromatography of extracts of particles is discussed.

70-1791 STOMACH CANCER AND AIR POLLUTION: AN EXPERIMENTAL STUDY IN A PETROCHEMICAL AREA. (E.) Neal, J. (U. Texas Med. Branch, Galveston) and R. H. Rigdon. Texas Rep. Biol. Med. 27(3):787-793, 1969.

The effects of various air pollutant particles (carbon black, lamp black and air particulates; all containing 3,4-benzpyrene (BP) and incorporated into the diet) on development of gastric cancer in 83 CFW mice were studied. The number of resultant tumors was small (8/83) due to the low BP content in the air samples. This experimental model may be useful in a clinical or epidemiologic study of gastric cancer in an

air-polluted area since it may be more significant to experimentally induce gastric tumors by feeding air particulate matter than to demonstrate a statistical relationship between gastric cancer and air pollutants.

70-1792 CARCINOGENIC HYDROCARBON CONTENT OF SUNFLOWER SEEDS. (Rus.) Kalinina, I. A. (N. N. Petrov, Sci. Res. Inst. Oncol., Leningrad, USSR). Vop. Onkol. 15(11):85-89, 1969.

The 3,4-benzpyrene (BP) content was determined for 6 types of sunflowers in 4 different geographic regions of the USSR with various climates. For all types of plants and all the various growing regions, the BP content was similar (ranged from 0-0.010 $\mu\text{g}/100\text{ g nuclei}$) and no correlation was found between BP content of seeds and the soil (which ranged from 0-6.4 $\mu\text{g}/\text{kg}$).

70-1793 MORPHOLOGICAL PECULIARITIES OF EXPERIMENTAL LUNG CANCER. (Rus.) Balenko, N. V. (Kiev Med. Inst., USSR). Vrach. Delo (4):17-20, 1969.

Rats were admin. 3,4-benzpyrene (BP in suspension; intratracheal admin./mo. $\times 10$) and lung changes reported. Admin. of 25, 2.5 or 0.5 mg BP resulted in the development of tumors in 3/40 (32.5% in 4-12 mo.), 6/28 (21.4% in 5-15 mo.) and 5/32 (15.6% in 9-18 mo.) rats, resp. Rats admin. 0.1 mg doses developed no tumors. Tumors were mostly squamous cell carcinomas and adenocarcinomas morphologically similar to human tumors, but with multicentric appearance, stimulated keratinization in the squamous cell types, and varied forms within the same animal (carcinomas with benign adenomatous proliferation). It is suggested that the polymorphic structure of various lung cancers demonstrates the transformation potential of cancer epithelium.

70-1794 HIGH-RESOLUTION AUTORADIOGRAPHIC LOCALIZATION OF 3,4-BENZPYRENE- ^3H IN MOUSE SKIN. (E.) Sobin, L. H. (WHO Cancer Unit, Geneva, Switzerland). Cancer Res. 30(4):123-128, 1970.

In 8-week-old Swiss mice treated by topical application of ^3H -3,4-benzpyrene (BP) to the skin, the disposition of the label was traced by autoradiography at intervals between 1 hour and 21 days. Sebaceous glands were the most heavily labeled site at 1 and 4 hours. While some degree of labeling was found in all components of the skin, that in the epithelial cells was greater than in other tissues. The dermis was lightly tagged, as were fat cells in the subcutis, while mature mast cells and underlying muscle had almost no labeled BP. Nuclei were labeled in proportion to their cytoplasmic label, but usually to lesser degrees. These

results corroborate earlier work on the binding of hydrocarbon carcinogens to soluble proteins and DNA, and support the idea that binding of carcinogen is proportional to cellular synthetic activity.

70-1795 INFLUENCE OF VITAMIN A AND 3,7-DIMETHYL-2,6-OCTADIENAL (CITRAL) ON THE EFFECT OF BENZO(a)PYRENE ON HAMSTER TRACHEA IN ORGAN CULTURE. (E.) Crocker, T. T. (U. California Sch. Med. Cancer Res. Inst., San Francisco) and L. L. Sanders. Cancer Res. 30(5):1312-1318, 1970.

Tracheas of 2-4-day-old Syrian hamsters were maintained in organ culture with combinations of 3,4-benzpyrene (BP; 10.5 $\mu\text{g}/\text{ml}$), 3,7-dimethyl-2,6-octadienal (citral; 2 or 4 mM) or vitamin A (VA; 0.01 or 0.02 mM) in the medium. Histological and autoradiographic study showed that C + BP combined produced epithelial squamous metaplasia by day 8, but did not alter replication, and was toxic at higher conc. The BP alone produced 1 squamous metaplasia by day 15. VA inhibited BP-induced epithelial cell differentiation, and when admin. alone produced shrinkage of cartilage matrix. C enhanced BP action on epithelial differentiation, but inhibited ciliary differentiation of columnar epithelium when admin. alone. A competitive interaction of VA and BP in respiratory epithelium, with a possible additive effect on cartilage, is suggested.

70-1796 DEMONSTRATION AND ORIGIN OF CARCINOGENIC POLYCYCLIC, AROMATIC HYDROCARBONS IN HUMAN AND ANIMAL ORGANS. (Ger.) Gräf, W. (Saranstr. 11, Erlangen, Germany). Arch. Hyg. Bakt. 153(5):390-396, 1969.

Mean conc. levels of 3,4-benzpyrene (BP; 0.38-0.68 $\mu\text{g}/100\text{ g dried tissue}$) were demonstrable at autopsy in the stomach, large intestine, lungs, liver, kidneys, heart and skeletal musculature of human subjects, aged 60-70 yr. Mean conc. levels in the blood, small intestine and spleen were 0.00, 0.04 and 0.20 $\mu\text{g}/100\text{ g dried tissue}$, resp. In 1- and 2-yr.-old pigs, mean conc. levels in the stomach and large intestine were 0.30 and 0.46 $\mu\text{g}/100\text{ g dried tissue}$, resp., with mean conc. levels in all the other organs studied ranging from 0.02-0.17 $\mu\text{g}/\text{g}$ and no BP demonstrable in the blood. The mean total conc. of BP in all the organs studied was about 2.5-fold higher in the human subjects. The indicated differences were attributed partially to the presence of life-long accumulations in the elderly human subjects and, in part, to the greater exposure of the humans to air pollution.

70-1797 THE INDUCTION OF MICROSOMAL O-DEALKYLATION BY A COMBINATION OF BENZO[A]PYRENE AND PHENOBARBITAL. (E.)

Creaven, P. J. (Texas Res. Inst. Mental Sci., Houston) and W. N. Reese, Jr. Chem. Biol. Interactions 1(2):238-240, 1969.

Admin. of various schedules of sodium phenobarbital (30 mg/kg body wt.; 2 admin./day x 4 days; in saline, i.p.) and 3,4-benzpyrene (BP; 20 mg/kg body wt; in sesame oil, as above) to male Sprague-Dawley rats (50 g). Livers were removed 24 hours after the last inj. and dealkylation activity was assayed. Dealkylation of 4-ethoxybiphenyl and 4-propoxybiphenyl was greatest with BP, and a combination of the 2 had additive results. The 2 compounds induced similar activity for dealkylation of 2-ethoxybiphenyl, and only phenobarbital induced dealkylation of 4-methoxybiphenyl. A combination of both made induction significantly less than for phenobarbital alone. Results for 2-methoxybiphenyl were similar. It is concluded that BP inhibits the induction of dealkylating activity produced by phenobarbital.

70-1798 3 : 4-BENZPYRENE-INDUCED IN VITRO FLUORESCENCE OF FETAL CELL LIPIDS IN THE DIAGNOSIS OF RUPTURED MEMBRANES. (E.) Montanari, G. D. (U. Padua, Italy), G. L. Grismondi and L. Zanoio. J. Obstet. Gynaec. Brit. Comm. 77(2):148-150, 1970.

In tests to diagnose rupture of placental membranes, in vitro treatment of amniotic fluid samples with 3,4-benzpyrene resulted in 1 false positive for 134 pts. with intact membranes and 1 false negative for 44 samples from pts. with transvaginal puncture or spontaneous rupture. All 18 amniocentesis samples had cells with characteristic bluish-white, silver fluorescence.

70-1799 EXPERIMENTAL STUDIES ON THE ABSORPTION AND DECOMPOSITION OF BENZPYRENE. (Ger.) Harke, H.-P., W. Döntenwill (Gazellenkamp 38, Hamburg, Germany) and W. Winkelmann. Z. Krebsforsch. 74(1):1-6, 1970.

Groups of male golden hamsters (80-100 g) and male Wistar rats (80-100) were inj. with 3,4-benzpyrene (BP; as a soln. in sesame oil or lutrol, or suspended in carboxymethylcellulose (CMC) and the BP content of tissues and organs was determined from 2-32 days later. Persistence of BP in the organism was dependent on the form of admin.; 4-6 days after inj. in sesame oil, 99% was either degraded or excreted. When BP was inj. as a suspension in CMC, 30% and 6% remained unchanged in form after 11 and 32 days, resp. Most of the BP was found in the abdominal cavity; 4 days after inj. 38.8% remained in the fatty and connective tissue of the abdomen, 1.05% in the liver, 0.1% in the kidneys and 3.2% remained in other parts of the animal. The rate of elimination was slower after admin. in lutrol than in sesame oil (probably due to BP crystallization and encapsulation in fatty tissue). The

rate of elimination also was dependent on the species of animal. Rats showed greater catabolic activity, particularly when sesame oil was the solvent.

70-1800 CARCINOGENIC HYDROCARBONS IN COFFEE SUBSTITUTES. (Ger.) Maier, H. G. (U. Frankfurt Inst. Food Chem., Germany) and W. Stender. Deutsch. Lebensmitt. Rdsch. 65(11):341-343, 1969.

In aqueous extracts of malt coffee, a commercial mixture of coffee substitutes, a commercial mixture of powdered coffee substitutes, and a chicory-based coffee substitute, the 3,4-benzpyrene (BP) content was 0.13-0.24 µg/kg, 0.06-0.10 µg/kg, 0.19-0.32 µg/kg and 0.18-0.40 µg/kg, resp. Comparable tabulations for 1,12-benzperylene were 1.1-1.9 µg/kg, 0.2-0.8 µg/kg, 0.6-1.1 µg/kg and 0.4-1.2 µg/kg, resp.; for fluoranthene (F), they were 2.2-4.0 µg/kg, 1.0-2.2 µg/kg, 2.4-3.0 µg/kg and 2.5-4.4 µg/kg, resp. When rye, barley, sugar beets and chicory were roasted for 30 min. at temperatures from 50°-240° C, the BP and F content increased as roasting temperatures increased from 100° C on, with very sharp increases at temperatures of 175° C and above. Chicory showed the highest content of both substances. In a related study, carefully roasted coffee substitutes contained relatively small amounts of BP as compared to other food-stuffs (beef, ham, fish, biscuits, bread crusts, true coffee, tea, chocolate, various vegetables and grain products).

70-1801 BINDING OF 7,12-DIMETHYLBENZ[a] ANTHRACENE TO DNA OF DIFFERENT ORGANS IN RATS. (It.) Prodi, G. (U. Bologna Inst. Gen. Path., Italy), C. Finzi and C. Franceschi. Boll. Soc. Ital. Biol. Sper. 45(1):26-29, 1969.

Female, adult Wistar rats were admin. ¹⁴C-7,12-dimethylbenzanthracene (DMBA; 9.31 mC/mmole; 25.5 µC in olive oil, i.p.) and the amount of bound DNA determined in 48 hours. Amounts of DMBA bound to DNA, measured in µmole/mg DNA, were 3.15, 1.94, 0.98 and 3.82 for liver, kidney, lung and spleen, resp.

70-1802 EFFECT OF ALCOHOL AND CIGARETTE SMOKE AS PROMOTING AGENTS IN HAMSTER POUCH CARCINOGENESIS. (E.) Elzay, R. P. (Virginia Commonwealth U. Med. Coll. Sch. Dent., Richmond). J. Dent. Res. 1200-1205, 1969.

Golden Syrian hamsters, 5 weeks old, were treated with 7,12-dimethylbenzanthracene (DMBA; 0.05% in mineral oil) and ethyl alcohol (EA; 50%) by topical application to cheek pouch epithelium. Whole cigarette smoke was applied to pouches of some of the hamsters (a half king size cigarette, 5 applications/week). After

5 days, pouch tissue was studied histologically. 17 animals treated with DMBA and combined EA and smoke developed 55 tumors, as compared to no tumors in smoke- or smoke + EA-treated animals. Results for DMBA + smoke or DMBA + EA were intermediate. It is concluded that whole cigarette smoke and EA act as promoting agents, rather than co-carcinogens or carcinogens, with smoke as the stronger promoting agent. A relationship between oral cancer and the ingestion of alcoholic beverages, smoking and exposure to atmospheric pollution is suggested.

1803 COMPOSITION STUDIES ON TOBACCO. XI. CARCINOGENESIS ASSAY OF SUBFRACTIONS OF THE NEUTRAL FRACTION OF CIGARETTE SMOKE CONDENSATE. (E.) Bock, F. G. (Roswell Park Mem. Inst., Buffalo, N. Y.), A. P. Swain and R. L. Edman. *J. Nat. Cancer Inst.* 44(6):1305-1310, 1970.

Male ICR Swiss mice, pretreated with 7,12-dimethylbenzanthracene (DMBA; 125 µg in 0.25 ml) by painting when about 60 days old, were administered various fractions (of the neutral fraction) of cigarette smoke condensate (0.25 ml; 5 admin./wk x 57 weeks). No tumors developed in 94 mice treated with acetone or DMBA + acetone (the negative controls). DMBA + croton oil treatment (positive controls) produced 259 tumors in 40/50 mice. The most polar subfraction and the benzene-toluene ether-dimethyl sulfoxide subfraction (which had most of the 3,4-benzpyrene) had the greatest tumorigenic effect; they produced tumors in 24/50 and 25/50 mice, resp., and each group had a total of 66 skin tumors. The polar subfraction was as active as 3,4-benzpyrene. The reconstituted fraction was less active than the original neutral fraction. Activity can possibly be attributed to tumor promoting material rather than to a complete carcinogen in the actions.

1804 CARCINOGENIC AND NONCARCINOGENIC POLYCYCLIC HYDROCARBONS IN *Neurospora crassa* AND CHINESE HAMSTER CELLS: THEIR PHOTODYNAMIC EFFECTS. (E.) Mallin, H. V. (Oak Ridge Nat. Lab., Tenn.) and E. H. Y. Chu. *Cancer Res.* 30(5):1236-1240, 1970.

Strains of *Neurospora crassa* were administered various polycyclic hydrocarbons such as 7,12-dimethylbenzanthracene (DMBA; 0.3 ml suspension of 1 µg/ml dimethylformamide), 1,2,3,4-dibenzanthracene, 2,5,6-dibenzanthracene, 3-methylcholanthrene (C), 3,4-benzpyrene (BP), 2-benzpyrene (2-BP) and benzanthracene (BA). UV radiation (1800 ergs/mm²/min.) followed immediately after first treatment. The carcinogens DMBA and BP, as compared to the noncarcinogen 2-BP, had a strong photodynamic effect. An exception in the results was BA, a weak carcinogen, which had a high photodynamic effect. Cultures of clone 9 of a Chinese hamster cell line were treated

by the same hydrocarbons in the dark x 24 hours, followed by exposure to black light (1275 ergs/mm²/min.). For the hamster cells the greatest photodynamic effect, which increased according to length of exposure to black light, was produced by DMBA and BP. It is suggested that DNA, important in carcinogenesis by polycyclic hydrocarbons, reacts with the products of the irradiation or catabolism of the hydrocarbons.

70-1805 SCINTILLOMETRIC AND AUTORADIOGRAPHIC DETERMINATION OF THE EXTRACTABILITY AND REMAINING ACTIVITY OF 9,10-DIMETHYL-1,2-BENZANTHRACENE IN EHRLICH ASCITES CELLS AFTER *IN VITRO* INCORPORATION. (Ger.) Amlacher, E. (Inst. Cancer Res., Berlin-Buch, Germany), A. Graffi, M. Schütt, V. Wunderlich and K. Schwabe. *Exp. Path.* 3(3):159-166, 1969.

Ehrlich ascites cells (5 x 10⁶ cells/ml; 8-10 days old) were incubated for periods of up to 21 hours with ³H-7,12-dimethylbenzanthracene (DMBA; 24-166 µC/ml), prior to lipid extraction and isolation of DNA and protein. Autoradiographic studies (A) and liquid scintillometry (S) yielded substantially identical results, with extracted radioactivity ranging from 98.6% to 99.5% at 21 hours for A and S, resp. Residual radioactivity was found bound to isolated DNA, RNA and protein in increasing amounts as the time of incubation was increased. Residual radioactivity was found in both the cytoplasm and the nucleus. In a prolongation of the experiment, maximal binding to DNA was found after 24-48 hr.

70-1806 FIBROADENOMAS IN PATIENTS RECEIVING ORAL CONTRACEPTIVES: A CLINICAL AND PATHOLOGIC STUDY. (E.) Fechner, R. E. (Baylor Coll. Med., Houston, Tex.). *Amer. J. Clin. Path.* 54(6):857-864, 1970.

Study of all cases of fibroadenoma, fibrocystic disease and primary carcinoma reported by The Methodist Hospital, Houston, between 1952-1969 showed the frequency of fibroadenomas to remain about the same (17.4%, 17.3%, 17.0% and 17.4% for the years 1952-56, 1957-60, 1961-64, and 1965-69, resp.) for a total of 4019 breast biopsies. The 54 fibroadenomas removed from pts. who received oral contraceptive therapy (5 began in 1961, 49 began in 1965) were compared with 54 fibroadenomas removed in 1955-56 (control group), prior to the availability of oral contraceptives. Four of the 54 fibroadenomas from pts. who had received oral contraceptives displayed acinar hyperplasia similar to fibroadenomas of pregnancy and 3 women in the 20-30-yr. age group had marked epithelial hyperplasia in breast tissue adjacent to the fibroadenomas. The remaining tumors and adjacent tissue revealed no other differences when compared to control fibroadenomas.

70-1807 EMBRYOPATHIC EFFECTS OF 7,12-DIMETHYLBENZ(A)ANTHRACENE AND ITS HYDROXYMETHYL DERIVATIVES IN THE SPRAGUE-DAWLEY RAT. (E.) Currie, A. R. (U. Aberdeen, Scotland), C. C. Bird, A. M. Crawford and P. Sims. Nature (London) 226(5249):911-914, 1970.

The effects of 7,12-dimethylbenzanthracene (DMBA) and its hydroxymethyl derivatives, 7-hydroxymethyl-12-methylbenzanthracene (7-OHM-12-MBA) and 12-hydroxymethyl-7-methylbenzanthracene (12-OHM-7-MBA), and a related benzanthrane derivative, 7-hydroxymethylbenzanthracene (7-OHMBA), admin. on days 2-18 of pregnancy were studied in the Sprague-Dawley rat and rat fetus. Results show that 7-OHM-12-MBA treatment on days 12-14 affected every fetus in each litter. The effects of DMBA and 7-OHM-12-MBA in the pregnant rat at day 8 or 13 of pregnancy were similar in many respects, but 7-OHM-12-MBA was the more potent embryopathic agent. Because DMBA and 7-OHM-12-MBA are embryopathic whereas 12-OHM-7-MBA and 7-OHMBA are not, it is suggested that for embryopathic activity, derivatives of benzanthrane must possess 2 active side-chains situated at C-7 and C-12, with an intact methyl group at C-12 being mandatory, and one of several possible substituents at C-7, of which a hydroxymethyl group seems to confer the most potent activity.

70-1808 STUDIES ON THE MECHANISM OF 7,12-DIMETHYLBENZ[a]ANTHRACENE LEUKEMOGENESIS IN MICE. I. STRAIN DIFFERENCE IN SUSCEPTIBILITY OF DMBA LEUKEMOGENESIS. (E.) Shisa, H. (Aichi Cancer Ctr. Res. Inst., Nagoya, Japan). Mie Med. J. 29(2):89-98, 1969.

Inbred mice, strains A/Jax, 129/J, AKR, C57BL/6JMs and SL/Ms and non-inbred Swiss/Ms were inj. s.c. at birth with 60 µg 7,12-dimethylbenzanthracene (DMBA) or 100 µg DMBA at 3 days of age. The frequency of DMBA-induced lymphomas significantly increased and the latent period significantly decreased compared to spontaneous cases. No significant difference was found in the leukemogenic response to DMBA given at birth or at 3 days and there were no sex differences. Most of the leukemias induced (80-92%) were thymic-type lymphomas; the gross and microscopic appearance is described. The order of susceptibility to DMBA induction of leukemia for the different strains of mice was Swiss, AKR, SL, 129 and C57BL; the A/Jax mice were rather refractory. Attempts to detect a leukemogenic virus in DMBA-treated Swiss mice were unsuccessful.

70-1809 STUDIES ON THE MECHANISM OF 7,12-DIMETHYLBENZ[a]ANTHRACENE LEUKEMOGENESIS IN MICE. II. THE ROLE OF THYMUS IN DMBA LEUKEMOGENESIS. (E.) Shisa, H. (Aichi Cancer Ctr. Res. Inst., Nagoya, Japan). Mie Med. J. 29(2):101-109, 1969.

Of 20 male and female Swiss mice, thymectomized (thmx.) and given 7,12-dimethylbenzanthracene

(DMBA; 100 µg, s.c.) at 3 days of age, 16 died of immunologic deficiency within 10 weeks and myeloid leukemia developed in 1/4 surviving animals. A thymic graft 1 week after thmx. or $5-8 \times 10^6$ viable spleen cells inoc. on days 10 or 17 after thmx. corrected the immunologic deficiency; 40/60 mice survived 10 weeks with no increase in the frequency of leukemia. Most (84%) of the newborn mice receiving 60 µg DMBA developed thymic leukemia within 6 mo.; this was reduced to about 21% in mice thmx. at 20 or 35 days of age. There was no restoration of leukemia frequency after implantation of 1-day-old isogenic thymus or autochthonous thymus. A morphological difference between leukemias in thmx. mice and thmx. mice with thymus grafts is described. No (0/16) thymus grafts from 20-day-old mice inj. with DMBA at birth and 3/58 grafts from 35-day-old mice produced local tumors or generalized leukemias after transplantation. It is concluded that the thymus induces lymphocytic maturation of leukemic cells.

70-1810 STUDIES ON THE MECHANISM OF 7,12-DIMETHYLBENZ[a]ANTHRACENE LEUKEMOGENESIS IN MICE. III. ACCELERATION OF DMBA LEUKEMOGENESIS IN MICE BY PRETREATMENT OF CORTISONE ACETATE. (E.) Shisa, H. (Aichi Cancer Ctr. Res. Inst., Nagoya, Japan). Mie Med. J. 29(2):111-121, 1969.

Pretreatment of Swiss mice with cortisone acetate (0.2 mg, i.p. at birth) before s.c. admin. of 7,12-dimethylbenzanthracene (DMBA; 100 µg) resulted in only a slightly greater frequency of lymphoma compared to those treated with DMBA alone, but reduced the latent period by 20-30 days. A significantly increased frequency of lymphoma was seen in cortisone-DMBA treated inbred A/Jax and C57BL mice along with a reduction in the latent period of 10-20 days. Lymphoma incidence in Swiss mice was reduced when the treatment sequence was reversed, or both agents were given simultaneously at birth. In newborn Swiss and C57BL mice treated with cortisone acetate (0.2 mg and 0.15 mg, resp.), a reduced wt. of the thymus, body and spleen was noted along with a depletion of small lymphocytes and an increase in the thymic large lymphocyte/small lymphocyte ratio. Impairment of immunologic response in treated animals lasted as long as 7 weeks.

70-1811 ASSOCIATION OF CANCER AND LEUKEMIA. (Rus.) Slinchak, S. M. (Kiev Inst. Clin. Exp. Oncol., USSR). Vrach. Delo (4):28-31, 1969.

Random-bred, 3-mo.-old, female rats were admin. 7,12-dimethylbenzanthracene (DMBA; i.v.) or were partially oophorectomized (oox.) and admin. DMBA. Of the normal and oox. rats, 35/50 and 40/50, resp., survived. After 200 days, 28/35 (80%) DMBA-treated rats developed tumors; of these, 17/28 (48.57%) were mammary tumors (9/17 single,

17 multiple). All DMBA-treated, oox. rats developed tumors; 35/40 (87.5%) had 143 mammary tumors, 4/40 had mammary cancer + leukemia (after removal of single and multiple tumors in 1 and 3, sp.), and 1/40 developed leukemia only (2/5 were myeloid leukemias). Of 173 pts. with various multiple neoplasms, 2 had leukemia associated with cancer. For a 57-yr.-old woman with chronic leukemia, stomach tumor and metastasis to the ovary, possible hormonal disorder and the simultaneous effect of carcinogenic agents are suggested. In a 51-yr.-old man with different malignant tumors and leukemia, the possibility of an etiological factor which simultaneously causes development of cancer in different tissues and systems is suggested.

70-1812 DIFFERENTIATION OF SALIVARY GLAND EPITHELIUM OF ALBINO RATS IN EXPERIMENTAL CARCINOGENESIS. (Rus.) Rybakova, M. G. P. Pavlov 1st Med. Inst., Leningrad, USSR. p. Onkol. 15(4):62-66, 1969.

Random-bred, male albino rats were treated with 7,12-dimethylbenzanthracene (DMBA; 3 mg pellets implanted in the submaxillary gland) and sacrificed 3-10 mo. later. Tumors developed in 1/40 rats; they were histologically classified as carcinoma (20), lymphoma (3) and rhabdomyosarcoma (1). Of the carcinomas, 8/20 were squamous cell-type, 5/20 were adenocarcinomas and 7/20 were carcinoma with double differentiation of the epithelium.

70-1813 CERVICAL LYMPH NODE METASTASIS OF HAMSTER CHEEK POUCH CARCINOMA INDUCED BY DMBA. (E.) Rwomushana, J. W. (Hadassah U. Hosp., Jerusalem), A. Polliack and I. S. Levij. Dent. Res. 49(1):184, 1970.

Metastases from a right cheek pouch squamous cell carcinoma were found in cervical lymph nodes on the contralateral side in 1/10 hamsters admin. 7,12-dimethylbenzanthracene (DMBA). The animal was treated with 3 applications/week of 0.5% DMBA for 12 weeks, then 0.0225% vinblastine (admin./week x 6 weeks). No other metastases were seen in 562 hamsters treated with DMBA.

70-1814 INCIDENCE OF INDUCED TUMORS IN THE RAT SUBMANDIBULAR GLAND WITH DIFFERENT DOSES OF 7,12-DIMETHYLBENZ-(α)-ANTHRACENE. (E.) Schmutz, J. A. (State U. New York, Buffalo) and P. Chaudhry. J. Dent. Res. 48(6):1316, 1969.

Male, 2-3-mo.-old Sprague-Dawley rats were admin. 7,12-dimethylbenzanthracene (single 250- μ g inj., or 2 x 250 μ g in the right submandibular gland) and tumors developed in 38-45% after 20 weeks. All 11 animals admin. a single 200 μ g dose developed tumors. All but 3 tumors were squamous cell carcinomas with no metastases to the lungs, liver or kidneys.

70-1815 TUMOR INDUCTION AND RESORPTION OF 7,12-DIMETHYLBENZ-(α)-ANTHRACENE AFTER ITS SINGLE APPLICATION TO MOUSE SKIN. (Rus.) Andrianov, L. A. (Inst. Exp. Clin. Oncol., Moscow) and V. S. Turusov. Vop. Onkol. 15(12):64-68, 1969.

In female (C57BL x CBA) F₁ mice admin. 7,12-dimethylbenzanthracene (DMBA; 25-1600 μ g in benzene), topical application to dorsal skin had a toxic effect and the number of papillomas induced was dose-dependent. First papillomas appeared after 36 weeks in 1/20, 1/19 and 2/21 survivors for doses of 25, 50 and 100 μ g, resp.; they appeared after 4 weeks in 4/35, 5/31, 3/32 and 6/32 survivors for doses of 200, 400, 800 and 1600 μ g, resp. A direct relationship between carcinogenic effect and duration of characteristic DMBA fluorescence was observed.

70-1816 RAPID INDUCTION OF SUBCUTANEOUS FIBROSARCOMA BY 7,12-DIMETHYLBENZ-(α)-ANTHRACENE IN AN INBRED LINE OF SYRIAN HAMSTERS. (E.) Homburger, F. (Bio-Res. Inst., Cambridge, Mass.) and S.-S. Hsueh. Cancer Res. 30(5):1449-1452, 1970.

Admin. of a single inj. of 7,12-dimethylbenzanthracene (DMBA; 500 μ g in 1.0 ml tricaprilyn, s.c.) to 90-day-old Syrian B10 hamsters was followed by an av. latency period of 13-16 weeks before tumor appearance in 9/10 inbred strains. In contrast, av. latency for 1/10 strains (Warren hamsters highly susceptible to DMBA) was 10 weeks; this difference was statistically significant. Tumors were fibrosarcomas invading the s.c. musculature, with no morphological differences between strains.

70-1817 STUDIES ON THE MECHANISM OF SKIN TUMOR PROMOTION. (E.) Hennings, H. (U. Wisconsin Med. Ctr. McArdle Lab. Cancer Res., Madison) and R. K. Boutwell. Cancer Res. 30(2):312-320, 1970.

Application of 0.5% croton oil to the backs of skin tumor-sensitive female mice induced a 2-3-fold increase in the uptake of ³H-cytidine (max. at 6 hours) and leucine (12 hours), and a 60% decrease in labeled thymidine uptake which was followed by a 3-fold increase at 18 hours. The stimulation of DNA synthesis was not affected by pretreatment with 7,12-dimethylbenzanthracene (DMBA). When 50 μ g cantharidin, a weaker promoting agent than croton oil, was applied to the skin of mice, both DNA and RNA synthesis was stimulated, especially the rapidly-labeled fraction of RNA (although to a lesser degree than by croton oil). In mice wounded 6 weeks after the admin. of 7 μ g DMBA, 37% developed papillomas along the wound line, and 58% developed tumors when wounded after 16 weeks.

70-1818 EARLY HISTOLOGICAL CHANGES OF THE NERVOUS SYSTEM OF THE SKIN IN RABBITS AND MICE FOLLOWING APPLICATION OF DMBA SOLUTION, BENZENE AND ACETONE. (Pol.) Pawłowski, A. (Acad. Med. Derm. Clin., Warsaw), D. Olejnik, J. Bem and M. Roszczyńska. Przegl. Derm. 57(1):23-29, 1970.

Application of 7,12-dimethylbenzanthracene (DMBA; 1% soln.) or its solvents (benzene and acetone) to male, 5-7-mo.-old chinchilla rabbits (10 animals, 1 admin./week) and adult male white mice (32 animals, 2 admin./week) was followed by examination of the skin in 24-72 hours and 5-20 days. Changes considered characteristic of the response of the nervous system of the skin to application of DMBA included signs of degeneration of intraepidermal nerve fibers after 48 hours and hypertrophy and destruction of follicles and their nerve elements. After 72 hours, only nerve elements associated with the DMBA-painted areas of the skin had further degenerated.

70-1819 SOME HISTOCHEMICAL PECULIARITIES AND ULTRASTRUCTURE OF INDUCED BRAIN TUMORS IN RATS. (Rus.) Abdullakhodzhaeva, M. S. (Uzbek Sci. Res. Inst. Roentgen. Radiol. Oncol., Tashkent, USSR). Med. Zh. Uzbek. (10):50-56, 1968.

Implantation of 7,12-dimethylbenzanthracene (DMBA; 2 mg pellets) in the brains of rats resulted in the development of 5 histologically-different tumors in 3-7 mo.; detailed histochemical study of the tumors followed. The round and polygonal cells of the sarcomas were rich in RNA and -COOH groups; their nuclei showed large amounts of chromatin with DNA, proteins (P) and amino groups. Ependymoma cells had moderate amounts of -COOH groups and P, whereas ependymoblastomas had larger amounts of these. The microcellular astrocytomas displayed uniformity of elements and free location of cells, with both nucleus and cytoplasm showing moderate nucleic acid and P functional group content. Glioblastoma multiforme was characterized by variability and the giant cells were particularly rich in RNA, P and -COOH groups.

70-1820 NEPHROBLASTOMAS INDUCED IN OVARECTOMIZED RATS BY DIMETHYLBENZANTHRACENE. (E.) Jasmin, G. (U. Montreal Fac. Med., Quebec, Canada) and J. L. Riopelle. Cancer Res. 30(2):321-326, 1970.

Female, 50-day-old Sprague-Dawley rats were admin. 2 doses of 7,12-dimethylbenzanthracene (DMBA; 10 mg each, over 4 days; by gastric tube). Some of the animals were oophorectomized (oox.) either 48 hours before or 2 weeks after DMBA admin. All 24 intact animals, surviving more than 3 mo., had mammary tumors with an av. time of appearance of 2.74 mo. Of the surviving oox. rats, 11/56 (20%) developed mammary tumors in an

av. time of 4.95 mo. No significant difference was seen for the 2 times of oox. Nephroblastomas were seen by an av. time of 6.03 mo. in 8/56 oox. rats only.

70-1821 EFFECTS OF A HYPOTHALAMIC ESTROGEN IMPLANT ON GROWTH OF CARCINOGEN-INDUCED MAMMARY TUMORS IN RATS. (E.) Nagasawa, H. (Michigan State U., East Lansing) and J. Meites. Cancer Res. 30(5):1327-1329, 1970.

Admin. of a single inj. of 7,12-dimethylbenzanthracene (DMBA; 5 mg, i.v.) to 55-day-old female Sprague-Dawley rats induced mammary tumors in 45-80 days. Four groups of rats were treated with the following implants: 1) estradiol benzoate (EB; 0.7-1.0 mg, with cholesterol (1:100) in a glass capillary tube) in the hypothalamic median eminence, 2) EB outside the median eminence, 3) EB in the cerebral cortex and 4) cholesterol in the median eminence. Significant differences were found only in the group treated with EB in the median eminence. They included an accelerated tumor growth rate, a linear increase in number and size of tumors and a greater total tumor wt. These are attributed to increased serum prolactin levels resulting from direct action of EB on the hypothalamus and pituitary body. The final body wt. for all treatments was about the same. It is suggested that the increased number of tumors may be due either to growth of established mammary tumor cells or to transformation of preneoplastic ones.

70-1822 OBSERVATIONS ON THE HORMONE SENSITIVITY OF 7,12-DIMETHYLBENZ(α)ANTHRACENE-INDUCED MAMMARY TUMORS IN THE SPRAGUE-DAWLEY RAT. (E.) Griswold, D. P., Jr. (Southern Res. Inst. Kettering-Meyer Lab., Birmingham, Ala.) and C. H. Green. Cancer Res. 30(3):819-826, 1970.

Single feeding of 7,12-dimethylbenzanthracene (DMBA; no details) to female Sprague-Dawley rats induced mammary tumors which were studied for hormone response and for the effects of steroid admin. on tumor regression after oophorectomy (oox.). Greatest tumor regression occurred in rats oox. 4 mo. after DMBA treatment; the regression decreased for the 5-, 6- and 7-mo. groups. Treatment with 2α-methyldihydro-testosterone propionate (MDTP; 10 mg/kg/day x 1-20 days) caused longest and greatest tumor regression in the 4- and 5-mo. groups. DMBA-fed rats were admin. MDTP (10 mg/kg/day x 1-40 days from day 30 of experiment) to delay appearance of tumors. Further hormone treatment (MDTP; 10 mg/kg/day x 1-20 days) or oox. caused no significant difference in tumor response compared to the groups with no hormone-delayed tumor development. In age and mass related studies with androgen treatment, large tumors of rats treated 180-210 days after DMBA admin. regressed

significantly less than small tumors. Studies of steroid effect on oox.-induced tumor regression showed that MDTP, testosterone propionate and diethylstilbestrol significantly lessened tumor progression; delayed treatment with the steroids, following oox., induced stimulated tumor growth.

-1823 THE EFFECT OF PORTACAVAL SHUNT ON 7,12-DIMETHYLBENZ(a)ANTHRACENE-PRODUCED MAMMARY CARCINOMA IN THE RAT. (E.) Reichle, A. (Temple U. Health Sci. Ctr., Philadelphia, Pa.), M. Gruenstein, D. R. Meranze, G. P. Rosemond and M. B. Shimkin. J. Surg. Res. 9(10):559-565, 1970.

Left-to-side portacaval shunts constructed 1 week before or 1 week after admin. of 7,12-dimethylbenzanthracene (DMBA; in 1.0 ml sesame oil, by stomach tube) to Holtzman rats resulted in a significant decrease of mammary carcinomas (4/17 and 3/14, resp.) compared to sham-operated (8/10) rats and controls (10/10). Using a 2-week interval between shunt and subsequent DMBA admin., again, a significant decrease in breast carcinoma was evident. Splenectomy had no effect on DMBA-induced mammary tumors. Several parameters, including changes in gastrointestinal absorption, hormonal conditions and wt. gain patterns may be altered after portacaval shunt, but their relation to the decreased tumor frequency is not known.

-1824 STUDIES OF THE KINETICS OF GROWTH AND REGRESSION OF 7,12-DIMETHYLBENZ(a)ANTHRACENE-INDUCED MAMMARY ADENOCARCINOMA IN SPRAGUE-DAWLEY RATS. Simpson-Herren, L. (Southern Res. Inst. Kettering-Meyer Lab., Birmingham, Ala.) and D. P. Griswold, Jr. Cancer Res. 30(3):813-818, 1970.

Female Sprague-Dawley rats with 7,12-dimethylbenzanthracene-induced mammary adenocarcinoma, the tumor cell cycle (about 20 hours) of S, G₁, G₂ and M phases of 8.5, about 11.5, about 1.0 and about 1.0 hours duration. The thymidine index (TI) was low (less than 10) in growing tumors, and was sharply reduced in tumors regressing after oophorectomy (oox.). The TI remained low during growth stasis in tumors regressing due to oox., and increased in spontaneously-recurring tumors. Oox. rats admin. progesterone (8 mg/day x 4 or 8 days, 30 days after oox.) and 17 β -estradiol (2 μ g/day, as above) had about a 10-fold increase in the TI.

-1825 LACK OF CORRELATION BETWEEN MORPHOLOGICAL AND BIOCHEMICAL PARAMETERS IN MAMMARY ADENOCARCINOMAS OF RATS INDUCED WITH 7,12-DIMETHYLBENZ(a)ANTHRACENE. (E.) Hilf, R. (U. of Rochester Sch. Med. Dent., N. Y.), H. Goldenberg, M. Gruenstein, D. R. Meranze and M. B. Shimkin. Cancer Res. 30(5):1223-1250, 1970.

Female, 51-day-old Sprague-Dawley rats were fed 7,12-dimethylbenzanthracene (5 mg in 1.0 ml sesame oil/week x 5 weeks, by stomach intubation) and animals with tumors examined for 42 days after appearance of tumor. Tumors were then separated on the basis of growth rate (wt. increase of less or more than 100 mg/day; 10 and 5 tumors, resp.) and evaluated histologically and biochemically. Significant differences between the 2 groups were seen for 3/21 different parameters, higher isocitrate dehydrogenase and hexokinase activities and lower triglyceride content in the faster-growing tumors. Although some biochemical coordination was evident, no correlation between the enzyme activities and rate of neoplastic growth was seen.

70-1826 UPTAKE AND CLEARANCE OF 9,10-DIMETHYL-1,2-BENZANTHRACENE-9-¹⁴C BY MAMMARY PARENCHYMAL CELLS OF THE RAT. (E.) Janss, D. H. (U. Tennessee Med. Units, Memphis) and R. C. Moon. Cancer Res. 30(2):473-479, 1970.

Virgin female 50-day-old Sprague-Dawley rats were admin. 7,12-dimethylbenzanthracene (DMBA; single 20 mg inj., p.o.) and ¹⁴C-DMBA (50 μ C), and the radioactivity in the abdominal-inguinal mammary glands was determined. The whole teat (mammary parenchyma and adipose tissue), the mammary gland fat cells and the mammary vascular component showed peak activity at 16 hours after feeding, which declined rapidly by 24 hours, especially the components with the smaller percentage of total lipid. Parenchymal cell intracellular lipid had a much higher specific activity but a similar pattern as parenchymal cells; both peaked at 6 hours, but the activity of the dry, fat-free parenchymal cells peaked at 16 hours. It is concluded that the carcinogen was taken up by the parenchymal cells simultaneously and independently of the fat cells, concentrating first in the intracellular lipid and then being released to the other cellular constituents.

70-1827 DETERMINATION OF 1,2-BENZANTHRACENE IN PETROCHEMICAL EFFLUENTS. (E.) Ershova, K. P. (Sov. Inst. Gen. Environ. Hyg., Moscow) and I. M. Mints. Hyg. Sanit. 33(7-9):371-374, 1968.

A method of determining polycyclic aromatic hydrocarbons is described where chromatographic fractions are dissolved in n-octane and the fluorescent spectra photographed at the temperature of liquid nitrogen. Comparison of the relative intensities of the spectral lines to a standard soln. showed that 1,2-benzanthracene has a standard deviation of 53% with a sensitivity of 0.25 μ g/ml.

70-1828 THE ROLE OF RIBONUCLEIC ACID AND PROTEIN SYNTHESIS IN MICROSOomal ARYL

HYDROCARBON HYDROXYLASE INDUCTION IN CELL CULTURE. THE INDEPENDENCE OF TRANSCRIPTION AND TRANSLATION. (E.) Nebert, D. W., and H. V. Gelboin (NCI, Bethesda, Md.). J. Biol. Chem. 245(1):160-168, 1970.

The possibility of a rate-limiting step involving the translation of an induction-specific RNA was investigated in the case of 1,2-benzanthracene (BA)-induction of aryl hydrocarbon hydroxylase in fetal hamster cell cultures. Protein synthesis inhibitors (cycloheximide or puromycin) or RNA synthesis inhibitors (actinomycin D or 2-mercapto-1-(β -4-pyridethyl)benzimidazole), when added simultaneously with inducer, completely prevented enzyme induction. When actinomycin D was added to BA-pretreated cells, enzyme activity continued to increase; this increase was prevented by addition of cycloheximide. Thus, the initial phase of microsomal enzyme induction appeared to be a translation-independent synthesis of RNA, followed by a transcription-independent phase of protein synthesis.

70-1829 HUNDRED DAY LEUKEMIA: PREFERENTIAL INDUCTION IN RAT BY PULSE-DOSES OF 7,8,12-TRIMETHYLBENZ(A)ANTHRACENE. (E.) Huggins, C. (U. Chicago Ben May Lab. Cancer Res., Ill.), L. Grand and H. Oka. J. Exp. Med. 131(2):321-330, 1970.

Female, 30-day-old Long Evans rats were admin. various hydrocarbons (35 mg/kg, in 5 pulse-doses biweekly; i.v.). By day 100, leukemia developed in 35/44 of those admin. 7,12-dimethylbenzanthracene, 8/10 admin. 7,8,12-trimethylbenzanthracene (TMBA), 2/9 admin. 6,8,12-TMBA, 1/14 admin. 7,9,12-TMBA and in none admin. either 5,7,12- or 6,7,12-TMBA. In rats admin. 7,8,12-TMBA, frequency of leukemia was directly related to number of pulse-doses. All 18 young female rats (that had at least 1 estrus) given a series of 4 pulse-doses developed mammary cancer in 42-98 days; of the 25-day-old rats admin. a series of 5 pulse-doses, 3/20 had mammary cancer and 19/20 developed leukemia, mostly stem-cell type associated with erythroblastosis. Clinical and histological characteristics of the leukemias are also described.

70-1830 LONG-TERM TOXICOLOGIC AND TUMORIGENESIS STUDIES ON AN ORAL CONTRACEPTIVE AGENT IN ALBINO RATS. (E.) Schardein, J. L. (Parke Davis Co., Ann Arbor, Mich.), D. H. Kaump, E. T. Woosley and M. M. Jellema. Toxic. Appl. Pharmacol. 16(1):10-23, 1970.

Doses of an oral contraceptive (98% norethindrone, 2% ethynylestradiol; 0.3-0.4 and 3-4 mg/kg/day x 2 yr., p.o.) admin. to 7-8-week-old Sprague-Dawley albino rats were 10-100-fold greater than recommended human intake. No significant difference in tumor development was seen for controls and treated rats; the number of tumors which

developed (327 in controls, 372 in treated animals) was not significantly different in females at either dose level or males at low dose levels. Males at high dose schedules developed a significantly greater number of tumors. Treatment decreased development of adrenocortical and pancreatic adenomas and subcutaneous fibrosarcomas, but increased occurrence of neoplasms of the liver, uterus, pituitary and mammary gland. Other results included decreased mortality rate, with greater survival and better health among treated rats than controls toward the end of the experiment, hair loss more predominant in females and increased liver weight in treated animals. There was evidence of diffuse hyperplasia of the liver, gonadal atrophy in treated males, and squamous metaplasia of the endometrium in treated females. It is suggested that the results are directly related to the biological activity of the components of the contraceptive agent.

70-1831 HISTOLOGICAL MODIFICATION OF FIBRO-ADENOMA OF THE BREAST ASSOCIATED WITH ORAL HORMONAL CONTRACEPTIVES. (E.) Brown, J. M. (Inst. Med. Vet. Sci., Adelaide, Australia). Med. J. Aust. 1(6):276-277, 1970.

A 25-yr.-old woman presented with a 2-cm lump in her right breast which she had noticed for 1 mo. and which clinically and macroscopically appeared like a fibroadenoma. Histological examination revealed an atypical fibroadenoma with exaggerated epithelial proliferation consisting of irregular islands of uniform cells separated by a dense connective tissue stroma. Occasional mitosis and secretory activity, but no anaplasia, were also seen. She reported having taken the oral contraceptive Norlestrin for 10 mo. before a pregnancy which was terminated by the delivery of a stillborn, anencephalic infant at 9 mo. She then took Lyndiol for 1 yr., had a normal pregnancy and was again taking Lyndiol for 4 mo. prior to the discovery of the breast lump.

70-1832 COMPARISON OF TUMORIGENESIS AND OF LONG-TERM DEVELOPMENT OF OVARIAN AUTO-GRAFTS ON THE GREATER OMENTUM OF CASTRATED INFANTILE AND MATURE RATS. (E.) Ber, A. (Beilinson Hosp. Rogoff-Wellcome Med. Res. Inst., Petah Tikva, Israel). Cancer Res. 30(2):426-429, 1970.

Oophorectomy was performed on 3-week-old and 14-week-old albino rats (total 125 and 129, resp.), and fragments of the ovary implanted near the stomach. The autografts developed in all animals, but grew significantly faster and were less prone to fatty degeneration in the younger rats. Granulosa tumors were detected in both groups at 6 mo. (more frequently in the younger animals); and after 12 mo., the mean wt. of tumors was significantly higher in the younger rats. At every time interval for both

groups, mean wt. of tumor-bearing implants was higher compared to implants without tumors.

-1833 CHARACTERISTICS OF AN ANDROGEN/ESTROGEN-INDUCED UTERINE SMOOTH MUSCLE CELL TUMOR OF THE SYRIAN HAMSTER. (E.) Kirkman, H. (Stanford U. Sch. Med., Calif.) and F. T. Algard. Cancer Res. 30(3):794-800, 1970.

Male and female golden Syrian hamsters were given min. diethylstilbestrol (0.11 mg/day, by subcutaneous pellet implant or inj.) and testosterone propionate (0.15 mg/day, as above). Primary leiomyosarcomas of the uterus and some autonomous variants were transplanted serially to untreated animals or intact or gonadectomized hamsters treated with androgen, estrogen or androgen + estrogen. Short periods (100-200 days) of treatment retained the typical tumor pattern, whereas long periods (250-350 days) resulted in atypical pattern and marked anaplasia and giant cell formation. After transplant growth was established, when androgen + estrogen was cut off, an initial decrease in transplant size was followed by renewed growth. The uterine tumor transplants rapidly became autonomous. It is suggested that such tumor growth can be retarded, but not prevented, by hormones.

-1834 BREAST CANCER IN A MAN TREATED WITH DIETHYLSTILBESTROL. (E.) O'Grady, P. and R. W. McDivitt (525 E. 68th St., New York, N. Y.). Arch. Path. (Chicago) 88(2):162-165, 1969.

67-yr.-old man presenting with carcinoma of the prostate was admin. diethylstilbestrol (30 mg/day initially, decreased to 5 mg/day x 10 mo., 10 mg/day x the next 3 yr. and 20 mg/day x 2 yr.). At the end of this 6-yr. course, Paget's disease of the right nipple was diagnosed accompanied by progressive gynecomastia and excoriation for 5 and 2 yr., resp. A right radical mastectomy was performed. The presence of infiltrative, scirrhous-type carcinoma surrounding the ducts containing *in situ* carcinoma precludes the possibility that the breast tumor was a metastasis from the prostate carcinoma. Marked terminal duct hyperplasia with true lobule formation and intraluminal secretions was observed in breast tissue surrounding the tumor. It is believed that the observed lobular atypia was caused by the migration of tumor cells into lobules from cancer-containing ducts rather than a change in the intrinsic lobular epithelium.

-1835 SEX HORMONES AND CARCINOMA OF THE LARYNX IN WOMEN. (Ger.) Hanson, J. (Martin Luther U. Ear Nose Throat Clin., Halle (Saale), Germany), L. Eckert and H. Mlytz. Ch. Klin. Exp. Ohr. Nas. Kehlkopfheilk. 33(3):277-286, 1969.

Determinations of urinary excretion levels of the C-17-ketosteroids, as a measure of androgen production, were made in 11 healthy controls and 10 women who had been treated 1-20 yr. previously for carcinoma of the larynx. Also determined were the urinary excretion levels of estradiol, estriol and estrone, as well as the presence of masculine or feminine distribution of body hair, voice quality, current gynecologic status and medical history. There was no evidence that tobacco played a carcinogenic role in these pts., nor were there significant differences, as compared to controls, in terms of gynecologic history, onset of menopause or menstrual difficulties. Although the mean estrogen levels of the pts. showed no significant differences as compared to controls, a significantly increased production of androgens was seen. An increased incidence of masculine distribution of body hair and of lowering of the pitch of the voice was also seen; both phenomena were confirmed present prior to carcinogenesis. It is concluded that the etiology of the tumor probably includes a complex endocrinologic disturbance, in which the sex hormones play a considerable part.

70-1836 PREMALIGNANT CHANGES OF THE CERVICAL, UTERINE AND VAGINAL EPITHELIUM OF MICE INDUCED BY INTRAVAGINAL ADMINISTRATION OF PLASTIC SPONGE. (Rus.) Vol'fson, N. I. (Sci. Res. Inst. Oncol., Leningrad, USSR). Biull. Eksp. Biol. Med. 34(4):91-95, 1969.

Prolonged, systematic intravaginal admin. of sponge particles (1 mg; 2 applications/week x 10-20 mo.), prepared from polyurethane (PU) or from butadiene carboxylate latex (BCL; an artificial polymer of rubber), to female CC57W mice was accompanied by the appearance and gradual progression of premalignant changes in the uterine cervix and vagina. Initial changes were absent in the PU group (duration of experiment, 322-596 days), while 23/23 showed premalignant changes, and 19/23 had symptoms of "pseudoerosion." In the BCL group (314-617 days), initial changes were present in 1/18, while 17/18 showed premalignant changes (8/17 with symptoms of "pseudoerosion," 3/17 with "pseudoerosion" and possible malignant transformation). In both groups, pathological changes progressed to only endophytic focal epithelial proliferation; papillomas apparently did not grow after 2-3 mo. Vaginal epithelium showed invasive growth and gradual "redifferentiation" with ingrowth into subjacent connective and muscle tissue, accompanied by the appearance of glandular-like structures. Irregular WBC infiltration of vaginal connective tissue was also seen.

70-1837 CARCINOGEN-INDUCED MAMMARY TUMORS FROM PRENEOPLASTIC NODULE OUTGROWTHS IN BALB/c MICE. (E.) Medina, D. (Baylor Coll.

Med., Houston, Tex.) and K. B. DeOme. Cancer Res. 30(4):1055-1059, 1970.

The effects of urethan (U; 0.2 ml of a 10% soln., 1 inj./week x 10 weeks, i.p.), 7,12-dimethylbenz-anthracene (DMBA; 0.2 ml of a 0.25% soln., 1 admin./week x 3 weeks, p.o.) and γ -irradiation (450 r) on the tumor-production of mammary tumor virus (MTV)-negative, nodule-inducing virus-negative, D series of BALB/c nodule outgrowth lines D1 and D2 were studied. All 3 agents increased tumor-producing capabilities of D1, and γ -irradiation did so in D2. (U and DMBA were not tested on D2). D1 treated with U or DMBA produced 45/59 (76%) and 16/25 (64%) tumors, resp., whereas irradiation produced 8/36 (22%) tumors and the untreated D1 had 1/74 (4%) tumors. Irradiation of outgrowth line D2 produced 61% tumors, compared to 14% tumors in untreated D2 controls. No MTV activity was found in blood from U- or DMBA-treated mice or in cell-free extracts of tumors arising in carcinogen-treated outgrowths. Neither Type A nor B virus particles were found in thin sections of carcinogen-treated outgrowths or tumors derived from carcinogen-treated outgrowths examined by electron microscopy.

70-1838 THE PREDICTIVE VALUE OF SKIN ALLOGRAFT SURVIVAL TIMES DURING THE DEVELOPMENT OF URETHAN-INDUCED LUNG ADENOMAS IN BALB/c MICE. (E.) Lappé, M. A. (U. California Cancer Res. Genet. Lab., Berkeley) and R. T. Prehn. Cancer Res. 30(5):1357-1361, 1970.

Urethan (U; 0.1 ml of 1% soln. in 0.85% NaCl soln.; i.p.) was inj. into 4-day-old male and female BALB/cCrGl mice and 2 mo. later the mice received skin grafts from female DBA/2CrGl mice. Although allograft survival was increased for some U-treated mice, particularly the males, such group differences were not significant because of widespread rejection scores. A skewed or flattened distribution of the number of mice versus rejection time indicates a slight effect of U on allograft survival. Division of mice into slow and fast rejection groups showed multiple tumors associated usually with the slow rejectors (10/23 and 3/13 mice, resp.). Also, newborn BALB/c AnNlcr mice were thymectomized (thmx.) and inj. with U (1.0 mg, i.p.) when 4 days old. Males received skin transplants from female DBA/2Helcr mice. Previous allografts were recorded for 6/8 mice killed prematurely which had longest allograft survival time and large respiratory adenomas. A male that rejected graft after 19 days died with a dorsal skin papilloma. There were significantly more tumors in thmx. mice 17 mo. after U treatment, as compared to controls (5.25 and 3.45 adenomas/mouse, resp.). Size of lung adenoma was significantly greater in thmx. males. It is concluded that number and size of lung tumors in U-treated mice correlates highly with allograft survival time.

70-1839 TUMOR INCIDENCE AND CELLULARITY IN LUNGS OF MICE GIVEN VARIOUS DOSE SCHEDULES OF URETHAN. (E.) White, M. R. (U. California Donner Lab., Berkeley), A. Grendon and H. B. Jones. Cancer Res. 30(4):1030-1036, 1970.

Female A/Jax mice (4.5, 6.5 and 8.5 weeks old) were admin. urethan (U; 1 inj. of 0.5 or 1.0 mg/g, or 2 inj. of 0.5 mg/g at 6-day intervals), and induction of lung tumors was assessed. There was no significant difference in tumor occurrence among the 3 ages at 1.0 mg/g of U. There was a reduction in tumor yield as a result of fractionation; that is, 2 doses of 0.5 mg/g admin. 6 days apart yielded fewer tumors than admin. of 1 dose of 1.0 mg/g. An age effect was noted for the 0.5 mg/g dose, as older mice had fewer tumors than younger ones. No hyperplasia of alveolar cells in the lung was observed, but cellularity unit vol. of lung changed with age. The number of cells correlated inversely with the alveolar space in fresh lung.

70-1840 EVALUATION OF DIMETHACRINE AND AZAPROPAZONE BY MEANS OF A MOUSE TEST FOR CARCINOGENIC ACTIVITY. (Ger.) Adrian, R. W. (Siegfried Co., Zofingen, Switzerland) and U. Jahn. Arzneimittelforschung 19(12):1997-1998, 1969.

When newborn mice of an unspecified strain were treated with 9,9-dimethyl-10-dimethylamino-propylacridan hydrogen tartrate (dimethacrine; 0.625 mg in a 1% gelatin soln., single s.c. inj.) or with 3-dimethylamino-7-methyl-1,2-(n-propylmalonyl)-1,2-dihydro-1,2,4-benzotriazine (azapropazone; 0.625 or 1.25 mg in a 1% gelatin soln., single s.c. inj.), neither compound showed any evidence of carcinogenic activity during a 1-yr. observation period. Animals treated with urethan (U; 1 mg in a 1% gelatin soln., single s.c. inj.) showed a 90.6% frequency of pulmonary adenomas, as compared to 17.5% in controls receiving the gelatin soln. alone and 6.7% and 6.4%, resp., in animals treated with the 2 test compounds above. In addition, 1 U-treated animal developed a lymphoma.

70-1841 ABSENCE OF THYMIC INVOLVEMENT IN THE INHIBITION OF URETHAN LUNG ADENOMAGENESIS BY X-RADIATION. (E.) Bartlett, G. L. (Inst. Cancer Res., Philadelphia, Pa.). Int. J. Cancer 5(3):384-388, 1970.

Thymectomy of male (DBA/2 x BALB/c)F₁ mice was followed by radiation (total 850 R) and inj. of bone marrow (i.v., 4 hours later) from syngeneic mice. Mice were then admin. urethan (U; 10% soln., 0.25 ml/week x 6 weeks, then 0.30 ml/week x 14 weeks; i.p.). Some mice received whole thymus grafts s.c. (on 3 occasions, 1-8 weeks after irradiation). Autopsies at week 26 showed no inhibition of U-induced lung tumor formation

thymectomy, and that tumor development was dependent on the presence of intact thymus. so, the inhibitory effect of radiation was not reversed by grafting of normal thymus tissue.

-1842 EFFECT OF SUNFLOWER OIL IN DIFFERENT DEGREES OF OXIDATION ON THE TUMOR INDUCTION IN RATS BY 2-ACETYLAMINOFLUORENE. (Rus.) Sheslavova, M. Ia. (Inst. Nutrit., Moscow). p. Onkol. 15(4):66-70, 1969.

Male rats were admin. N-2-fluorenylacetamide (FAA; 3.5 or 6.0 mg/day x 17 mo.) alone or in combination with sunflower oil (S0; 10% of the diet, ranging in degree of oxidation from fresh to 3.5% oxidized); 48/48 rats developed tumors within 5-8 mo., and the groups treated with 2.0-3.5% oxidized S0 + FAA developed the greatest number of tumors, with more subsequent metastases, more multiple tumors, and at the highest rate. Tumors included hepatomas, adenocarcinomas of the liver, and tumors of the lung, salivary glands and stomach. In a second experiment, rats were admin. FAA (1.2-4.0 mg/day x 12 mo.) alone or in combination with S0 (as above) and 67/88 rats developed tumors within 6 mo. Frequency, multiplicity and rate of tumor development increased as the degree of oxidation of S0 increased, with similar types of tumors developing. It is concluded that pre-treated S0 acts as a cocarcinogen with FAA in the liver; fresh S0 has similar properties, but does not induce metastasis of primary tumors, as do FAA + oxidized S0, or FAA alone.

-1843 INHIBITION OF LIVER TUMOR FORMATION IN ADRENALECTOMIZED C3Hf MICE. (It.) Leonidis, A. (Aristotle U. Inst. Path., Thessalonika, Greece). Minerva Med. 61(34):1863-1868, 1970.

Male C3Hf/b mice were admin. N-2-fluorenylacetamide (FAA; in the diet x 50 or 80 weeks), adrenalectomized (adx.) and the number of hepatomas was observed. After 50 and 80 weeks, untreated controls had 36.3% and 53.3% spontaneous tumors, resp. Of the mice treated with FAA only, 47.6% and 94.3%, resp., had tumors. Untreated adx. mice had no liver tumors (1 in the 80-week group had a small nodule), and adx. mice treated with FAA had no tumors after 50 weeks, while 63.1% had hepatomas after 80 weeks (with adrenalectomy in 2 mice). It is concluded that adx. inhibits FAA induction of liver tumors.

-1844 SERUM LIPOPROTEINS OF RATS FED AN ESSENTIAL FATTY ACID-DEFICIENT DIET WITH N-2-FLUORENYLACETAMIDE. (E.) Narayan, K. A. (Illinois Burnside Res. Lab., Urbana). Cancer Res. 30(4):1185-1191, 1970.

Rats were maintained on an essential fatty-acid deficient diet with or without addition of

N-2-fluorenylacetamide (FAA; 0.005% or 0.03% x 1 yr.), and serum lipoprotein (SLP) patterns were determined by disc electrophoresis. During early stages of carcinogen admin., SLP patterns reflected a marked increase in high-density lipoproteins (HDL), while in later stages both low-density lipoproteins (LDL) and HDL were increased. In the terminal stages (at 51-52 weeks), sera from rats fed 0.005% FAA had increases of very-low density lipoproteins and HDL between 1- and 2-fold, whereas LDL increased from 2-4-fold. The large increase in LDL was due mostly to a lipoprotein component that possessed electrophoretic and ultracentrifugal characteristics similar to that of rat serum HDL₁. It is concluded that marked differences in rat SLP occur depending on whether cancer exists in the liver or in remote organs and tissues.

70-1845 ALTERED AND DISTORTED DNA FROM A PREMALIGNANT LIVER LESION INDUCED BY 2-FLUORENYLACETAMIDE. (E.) Epstein, S. M. (U. Pittsburgh Sch. Med., Pa.), E. L. Benedetti, H. Shinozuka, B. Bartus and E. Farber. Chem. Biol. Interactions 1(1):113-124, 1969/70.

N-2-Fluorenylacetamide was admin. to male white Wistar rats (150-200 g) in the diet. Then, all rats were fed a normal basal diet for a minimum of 4 weeks and DNA was extracted from hyperplastic and nonhyperplastic nodules of the livers. Protein and RNA accounted for less than 0.5% and 1-5%, resp., of the preparation. The DNA from hyperplastic liver had 3 specific differences from normal rat liver: 1) an altered UV absorption spectrum, 2) a fraction with a buoyant density different from normal liver DNA or DNA from surrounding nonhyperplastic nodules, and 3) a distinguishable appearance when seen by electron microscope, with irregularly shaped fibers and regions of strand separation. It is suggested that such altered DNA may be involved in a loss of metabolic regulation leading to irreversible cell growth, with a possible subsequent malignant development.

70-1846 RETENTION OF METABOLIC REGULATION IN THE HYPERPLASTIC HEPATIC NODULE INDUCED BY N-2-FLUORENYLACETAMIDE. (E.) Teebor, G. W. (New York U. Med. Ctr., N. Y.) and I. Seidman. Cancer Res. 30(4):1095-1101, 1970.

Male Sprague-Dawley rats were fed N-2-fluorenylacetamide (FAA; 0.06%) for 12 weeks; this induced hyperplastic liver nodules, which precede the appearance of hepatocellular carcinomas by several mo. The activities of 3 enzymes, glucose-6-phosphatase (G6Pase), tyrosine α -ketoglutarate transaminase (TKGT) and tryptophan pyrrolase (TP), were studied. All of the enzyme-regulatory mechanisms were mediated by corticosteroid. Induction of TKGT and TP by hydrocortisone sodium succinate (10 mg/100 g), increase in

G6Pase after a 24-hour starvation period and its induction by triamcinolone were all studied. Results indicated that the loss of enzymatic adaptive responses characteristic of Morris hepatomas was not found in hyperplastic nodules induced by feeding of FAA.

70-1847 INFLUENCE OF OROTIC ACID ON LIVER TUMORIGENESIS IN RATS INGESTING ETHIONINE, N-2-FLUORENYLACETAMIDE, AND 3'-METHYLDIMETHYLAMINOAZOBENZENE. (E.) Sidransky, H. (U. Pittsburgh Sch. Med., Pa.) and E. Verney. *J. Nat. Cancer Inst.* 44(5):1201-1215, 1970.

In one series of experiments studying the influence of orotic acid on liver carcinogenesis, female Sprague-Dawley rats (150-350 g) were fed orotic acid (OA; 1%) either 3 weeks before or in conjunction with ethionine (E; 0.25%) or adenine sulfate (AS; 0.25%). The second series had male rats treated with OA and N-2-fluorenylacetamide (FAA; 0.025%) or AS (as above); the third group of male rats were fed OA and 3'-methyl-4-dimethylaminoazobenzene (MeDAB; 0.06%). Rats fed OA, 3 weeks before or during E or FAA feeding, developed fewer carcinomas than those fed E or FAA alone. For MeDAB treatment, however, the same high incidence of liver carcinoma was seen for all groups. Feeding of OA for 3 weeks, and then E or FAA alone, in comparison to treatment with E or FAA only, resulted in 58% and 87% incidence, resp., of liver carcinoma; this indicates an inhibitory action of OA, even when it is no longer part of the diet. It is concluded that fatty liver is not necessarily a contributing factor to hepatic tumorigenesis.

70-1848 ISOLATION AND IDENTIFICATION OF A PARAMAGNETIC COMPLEX FROM THE LIVERS OF CARCINOGEN-TREATED RATS. (E.) Woolum, J. C. (Washington U., St. Louis, Mo.) and B. Commoner. *Biochim. Biophys. Acta* 201(1):131-140, 1970.

Electron spin resonance studies of liver tissue from adult male Holtzman rats fed N-2-fluorenylacetamide (FAA, no details) determined the presence of a paramagnetic complex induced when FAA and NO_2^{-1} or NO_3^{-1} are present. It is identified as a NO-Fe^{+2} complex with a thiol-containing protein. It is suggested that the paramagnetic complex may be functional in the process of inactivation of FAA because it reduces frequency of liver tumors.

70-1849 INDUCTION OF CEREBRAL GLIOMAS IN RATS WITH DIETARY LEAD SUBACETATE AND 2-ACETYLAMINOFLOURENE. (E.) Oyasu, R. (Presbyterian-St. Luke's Hosp., Chicago, Ill.), H. A. Battifora, R. A. Clasen, J. H. McDonald and G. M. Hass. *Cancer Res.* 30(5):1248-1261, 1970.

Male Charles River Wistar rats and male and female, cesarean-delivered Sprague-Dawley rats (all 5-8 weeks old) were admin. N-2-fluorenylacetamide (FAA; 0.03-0.07% in the diet with 1.6 or 3.2% indole) and lead subacetate (1.0% in the diet). In 988 rats, 25 gliomas and 3 extra-cerebral tumors were found (2 probable meningeal origin, 1 acoustic neurilemmoma). Tumors developed after about 52 weeks. Gliomas were most frequent in animals admin. lead subacetate. Induction was not further enhanced when combined with FAA. Cerebral freezing did not enhance tumorigenesis by FAA and gliomas were significantly more frequent in older animals (over 60 weeks old). As compared to 1 glioma found in controls, FAA induced a delayed increase in gliomas (5.5%) in rats over 60 weeks old.

70-1850 AETIOLOGY OF TUMOURS OF THE URINARY BLADDER. INDUCTION OF TUMOURS IN THE URINARY TRACT OF THE RABBIT BY AROMATIC AMINES. (E.) Wood, M. (U. Leeds Med. Sch., England). *Industr. Med. Surg.* 39(2):82-88, 1970.

Male and female, 6-mo.-old, New Zealand white rabbits were admin. N-2-fluorenylacetamide (FAA; 100 mg in 1.0 ml corn oil; 3 admin./week, p.o.), 4-biphenylamine (BPA; 100 mg, as above) or 2-naphthylamine (NA; 100 mg, as above) for up to 3 yr. From 4-64 weeks after treatment, progressive hyperplasia of the bladder, ureter and renal pelvis was evident; no tumors were found. After 65-178 weeks, 12/16 rabbits admin. FAA had bladder tumors. Also, 10 ureteric and 7 renal pelvic tumors were found. After 65-88 weeks, 1/4 rabbits had a bladder tumor after BPA admin. and NA-treated animals had no tumors. Urinary obstruction by ureteric stenosis was performed to determine influence of urinary stasis on tumor induction. All animals developed hydro-ureter and hydronephrosis, and calculi were present. Only 1 FAA-treated animal developed transitional cell carcinoma of the bladder. Surprisingly, the unobstructed ureters (with greater FAA exposure) showed no development of tumors.

70-1851 THE IN VIVO BINDING OF METABOLITES OF 2-NAPHTHYLAMINE TO MOUSE-LIVER DNA, RNA AND PROTEIN. (E.) Hughes, P. E. (Baker Med. Res. Inst., Prahran, Victoria, Australia) and R. Pilczyk. *Chem. Biol. Interactions* 1(3):307-314, 1969/70.

A single inj. of ^3H - β -naphthylamine (NA; 3.75 mg in arachis oil; i.p.) was admin. to young female CBA and C57 mice and the livers and kidneys were examined and assayed in 0-96 hours or 1, 2, 3 and 12 weeks. The levels of ^3H -NA binding to all forms of macromolecules (DNA, RNA and proteins) were greater for CBA mouse liver than

for C57 mouse liver. Values for the liver were greater than for the kidney, which is more resistant to the carcinogenic activity of NA. Binding was centrilobular for the liver and in the transitional epithelium of the kidney. There was no residual radioactivity bound to RNA protein after 12 weeks, whereas for CBA mouse liver DNA it was still 15% the max. level at that time.

-1852 INCREASED SELECTIVITY OF INTERACTION BETWEEN FLUORENYLAMINE CARCINOGENS AND LIVER PROTEINS DURING HEPATOCARCINOGENESIS. (E.) Sorof, S. (Inst. Cancer Res., Philadelphia, Pa.), E. M. Young, R. Z. McBride, C. B. Coffey and L. Luongo. Molec. Pharmacol. 5(6):625-639, 1969.

Adult, male CFN rats were admin. N-2-fluorenylacetylacetamide (FAA; 0.036% x 5, 13 or 15 weeks in the diet), then a single dose of ^{14}C -FAA (5.2-16.6 $\mu\text{C}/100\text{ g}$ body wt., p.o. or i.p.) or ^{14}C -N-hydroxy-FAA (same dosage as for ^{14}C -FAA), and soluble proteins of the livers and hepatocarcinomas were isolated and resolved by column electrophoresis. In comparison to controls, which showed non-specific, diffuse distribution of labeled liver proteins, FAA ingestion resulted in marked specificity of binding to liver proteins, indicating that FAA metabolites interact selectively with specific target proteins. In its admin. the more active metabolite, ^{14}C -N-hydroxy-FAA, similar specific proteins (termed h-njugates) were found in preneoplastic livers. Admin. of ^{14}C -FAA and ^{14}C -N-hydroxy-FAA to rats bearing FAA-induced hepatomas did not produce the specific protein conjugates.

-1853 N-HYDROXY-2-FLUORENYLACETAMIDE. REACTION OF THE CARCINOGEN WITH GUANOSINE, RIBONUCLEIC ACID, DEOXYRIBONUCLEIC ACID, AND PROTEIN FOLLOWING ENZYMIC DEACETYLATION OR ESTERIFICATION. (E.) King, C. M. (Michael Reese Hosp. Med. Ctr., Chicago, Ill.) and B. Phillips. J. Biol. Chem. 244(22):609-6216, 1969.

The competitive influence of various mononucleosides on the incorporation of N-hydroxy-2-fluorenylacetylacetamide (OHFAA; catalyzed by soluble preparations of rat liver) into RNA, indicated that guanine was the major site of reaction of the nucleic acid with the activated OHFAA derivatives. The products of guanosine were characterized by UV spectroscopy and thin-layer chromatography as 8-(N-2-fluorenylamino)guanosine and 8-(N-2-fluorenylacetylacetamido)guanosine, derivatives of OHFAA after deacylation and esterification, resp. Digestion of the adducts with phosphodiesterase and alkaline phosphatase indicated that C-8 of guanine was the site of adduct formation. Activated derivatives of OHFAA reacted with DNA and protein, as well as with RNA.

70-1854 N-HYDROXY-2-ACETYLAMINOFLUORENE SULFOTRANSFERASE: ITS PROBABLE ROLE IN CARCINOGENESIS AND IN PROTEIN-(METHION-S-YL) BINDING IN RAT LIVER. (E.) DeBaun, J. R. (U. Wisconsin Med. Ctr. McArdle Lab. Cancer Res., Madison), E. C. Miller and J. A. Miller. Cancer Res. 30(3):577-595, 1970.

One- and 3-methylmercapto-2-acetylaminofluorene (1- and 3-methylmercapto-AAF, resp.) were characterized as alkaline degradation products of protein-bound methion-S-yl derivatives of N-hydroxy-AAF in rat liver *in vivo*. The quantity of o-methylmercapto-AAF released from hepatic tissues was proportional to the i.p. dose of N-hydroxy-AAF, thus giving an assay for reactive forms of the carcinogen *in vivo*. Studies on the levels of N-hydroxy-AAF sulfotransferase activity in rat liver, as assayed *in vitro*, paralleled the amounts of o-methylmercapto-AAF released from livers of similarly treated rats after N-hydroxy-AAF admin. and the susceptibility to liver tumor induction by N-hydroxy-AAF. The strong correlation between the above results and the hepatocarcinogenicity of N-hydroxy-AAF under several conditions in the rat and other species suggests that AAF-N-sulfate is 1 of the final reactive and carcinogenic metabolites of AAF and N-hydroxy-AAF in rat liver.

70-1855 POSSIBLE ROLE OF THE GLUCURONIDE CONJUGATE IN THE BIOCHEMICAL MECHANISM OF BINDING OF THE CARCINOGEN N-HYDROXY-2-ACETYLAMINOFLUORENE TO RAT-LIVER DEOXYRIBONUCLEIC ACID *IN VIVO*. (E.) Irving, C. C. (VA Hosp., Memphis, Tenn.), R. A. Veazey and L. T. Russell. Chem. Biol. Interactions 1(1):19-26, 1969/70.

Male rats (250 g) were admin. ^{14}C - and ^3H -labeled N-hydroxy-2-fluorenylacetylacetamide (OHFAA; 7.8 mg in corn oil, i.p.) and after 16 hours the liver DNA and RNA were isolated. The N-acetyl group of OHFAA was retained by 75% of the fluorene residues bound to ribosomal RNA; in contrast, only 35% of the residues bound to DNA still had the N-acetyl group. It is suggested that the glucuronide of OHFAA is responsible for most binding (a pH-dependent reaction) of the compound to rat liver DNA *in vivo*.

70-1856 INHIBITING EFFECT OF RESERPINE AND FEMALE SENSITIVITY IN HEPATIC TUMOR INDUCTION WITH 2,7-DIACETAMIDOFUORENE IN SMA/MS STRAIN MICE. (E.) Kozuka, S. (Nagoya U. Sch. Med., Japan). Cancer Res. 30(5):1384-1386, 1970.

Male and female, 8-week-old SMA/MS mice were admin. N-2,7-fluorenyldiacetylacetamide (FDAA; 0.025% in the diet) to induce tumors and were then inj. with reserpine (R; 1 $\mu\text{g}/\text{g}$ body wt./week x 32 weeks, s.c.). Development of hepatic nodules

was greatly prevented by R inj., but more appeared in the females. Other groups of mice were oophorectomized (oox.) or orchietomized (orx.), admin. FDAA and inj. with either testosterone propionate (TP; 80 µg, 2 admin./week, s.c.) or estradiol benzoate (EB; 80 µ, as above). The control females and oox. females admin. EB developed the greatest number of hepatic nodules; control males had the least. Orx. males showed increased frequency of malignancy, whereas the effect of oox. on females was not significant. TP inj. seemed to have a slight protective effect on oox. female mice. It is concluded that R depresses tumor development, and that females are more sensitive to tumor induction, a reversal of previous reports.

70-1857 N,N¹-2,7-FLUORENYLENEBISACETAMIDE (2,7-F.A.A.)-INDUCED RAT BOWEL CANCER. (E.) Thompson, J. H. (U. California Sch. Med., Los Angeles). Irish J. Med. Sci. 2(12):565-583, 1969.

Induction of bowel cancer and related serotonin levels were studied in male Buffalo rats admin. N,N¹-2,7-fluorenylenebisacetamide (0.025 g of diet, for 8 mo.). Results are as follows: Of the 30 bowel cancers found in 25 rats, 3 arose from the pyloric antrum, 2 from the upper duodenum, 20 from the small bowel and 3 and 2, resp., from the ascending and descending colon. Hepatomas and cholangiocarcinomas developed in 88% of treated rats. Twenty-five of 30 (83%) tumors were found in the pyloric antrum and small bowel and 5/30 (17%) in the large intestine. Serotonin levels were generally significantly increased in nonmalignant mucosa of treated rats as compared to controls, and significantly reduced in cancer mucosa when compared to nonmalignant mucosa of the same rat and to controls. Lower serotonin levels in certain tumors suggests that this amine may be one factor involved in the carcinogenic process.

70-1858 TRANSPLANTABLE ADENOCARCINOMAS OF THE RAT KIDNEY POSSESSING DIFFERENT GROWTH RATES. (E.) Morris, H. P. (Howard U. Coll. Med., Washington, D. C.), B. P. Wagner and D. R. Meranze. Cancer Res. 30(5):1362-1369, 1970.

Male, 1.4-mo.-old Buffalo strain rats and 3.4-mo.-old females of the same strain were fed 4¹-fluoro-4-biphenylacetamide (BAA; 1.10 mM/kg). Transplantable kidney adenocarcinomas developed in 1 male and 2 females after 8.7 and 10.6 mo. of BAA admin., resp. Other tumors included hepatomas in the males and mammary tumors in the females. The growth rate was slow for the tumors and varied for each, with no evidence of metastases to the lung. Further studies on kidney tumor growth and regulation of glutamine metabolism in the kidney are suggested.

70-1859 TERATOGENIC AGENTS: MAMMALIAN TEST SYSTEMS AND CHEMICALS. (E.) DiPaolo, J. A. (NCI, Bethesda, Md.). Ann. NY Acad. Sci. 163(2):801-812, 1969.

The teratogenic effects of polyfunctional alkylating agents, especially those used in cancer chemotherapy including nitrogen mustard, TEM, chlorambucil, busulfan and cyclophosphamide, are discussed. Use of these agents in man has not produced the deleterious effects expected from animal experimentation. The teratogenic and carcinogenic effects of nitroso compounds (dimethylnitrosourea, methylnitrosourea and N-ethyl-N-nitrosourea) and aflatoxins are also reviewed. One example is presented of aflatoxin B₁ (4 mg/kg; i.p.) admin. to pregnant hamsters on day 8 of gestation with resultant malformed or resorbed fetuses. Aflatoxin treatment (1 mg/kg) of C3H mice gave no malformations and only some dead or resorbed embryos. It is concluded that the toxic effect of aflatoxin depends upon species of animal.

70-1860 THE EFFECT OF DIMETHYLNITROSAMINE, CARBON TETRACHLORIDE, BUTTER YELLOW AND CYCLOPHOSPHAMIDE ON AMINO ACID INCORPORATION INTO FRACTIONS OF LIVER HOMOGENATE AFTER IN VITRO METABOLIC ACTIVATION. EVALUATION OF HEPATOTOXIC ACTION. (Ger.) Schnitger, F. (U. Tubingen Pharmacol. Inst., Germany) and H. Uehleke. Arch. Toxik. 25(2):169-182, 1969.

Incorporation of ¹⁴C-leucine into proteins of liver homogenates and the supernatant and microsomal fractions from male FW 40 albino rats (100-150 g) pretreated with phenobarbital (80 mg/kg i.p. x 5 days before death) was not affected by 4-N,N-dimethylaminoazobenzene, 4-N,N-dimethylaminoazobenzene-N₁-oxide, dimethylnitrosamine, carbon tetrachloride and cyclophosphamide (2 µmoles/ml). Addition of a reduced nicotinamide adenine dinucleotide phosphate (NADPH₂) regenerating system into the incubation mixture caused rapid metabolism of these substances, but did not inhibit leucine incorporation. Neither leucine incorporation nor the polyuridylic acid-directed incorporation of ¹⁴C-phenylalanine was affected by prior incubation of microsomes with NADPH₂ and the toxic agents. By measuring the dealkylation of N-methylaniline to aniline, the speed of metabolism (activity of mixed-function oxidases) in the different fractions was determined. The dealkylation was more rapid in the liver homogenate (16% after 10 min.), supernatant (8.8%) and complete leucine incorporating system with microsomes (6%) than in isolated microsomes (3.6%). It is concluded that these subcellular systems are not suitable models for the study of toxic action of substances on protein synthesis in intact cells and organs.

-1861 EFFECT OF VARIOUS TYPES OF CARCINOGENS ON THE HATCHING OF *Artemia salina* EGGS. u-Hoi, N. P. (U. Paris Radium Inst.) and P.-H. an. J. Nat. Cancer Inst. 44(4):795-799, 1970.

The effects of 14 compounds (13 known carcinogens and 1 closely-related derivative; in the medium) on the hatching process of brine shrimp eggs were determined. Influence varied according to chemical structure of the compound, but actual measure of carcinogenicity could not be determined. The 4-nitroquinoline-1-oxides were potent inhibitors, whereas 7,10-dimethylbenz(c)ridine was almost inactive. The nitrosamines exerted strong inhibitory effect to a definite stimulating effect on hatching by ethyl-N-methyl-nitrosocarbamate and 1-methyl-1-nitrosourea. Inhibition decreased as conc. increased for the latter carcinogen, DL-ethionine. A significant, near-cut difference was seen for the carcinogenic oxide, 1,2,3,4-diepoxybutane, and for 1,2,3,4-epoxycyclohexane which were inhibitory and completely ineffective, resp. The application of this fact for the biological screening of oxides is suggested. The mechanism of inhibition and activation of the egg hatching process by the various compounds is also discussed.

-1862 MUTAGENIC EFFECT OF A CARCINOGEN, 4-NITROQUINOLINE 1-OXIDE, IN BACTERIOPLASM T4. (E.) Ishizawa, M. (Kyushu U. Cancer Res. Inst., Fukuoka, Japan) and H. Endo. Mutat. Res. 9(1):134-137, 1970.

Bacteriophage T4 rII mutants in *E. coli* B culture were treated with 4-nitroquinoline 1-oxide (NQO; 100 µg/ml x 30 min.) and replated on *E. coli* KB, such that plaque formation of only wild-type (rII⁺) forms of the phage would occur. Comparison of plaque formation (both r⁺ and rII) on *E. coli* B showed reversion of the rII mutants to rII⁺ in vivo. In vitro studies with higher conc. of NQO (200 µg/ml) and extracellular rII phages showed no lethal or mutagenic effects. It is suggested that a guanidine:cytosine to adenine:thymidine base change is induced by NQO acting as an in vivo mutagen.

-1863 CHROMOSOMAL ALTERATION AND THE DEVELOPMENT OF TUMORS. XX. CHROMOSOMAL CHANGE IN THE COURSE OF MALIGNANT TRANSFORMATION IN VITRO OF HAMSTER EMBRYONIC CELLS BY 4-NITROQUINOLINE 1-OXIDE AND ITS DERIVATIVE, 4-HYDROXY-4-NITROQUINOLINE 1-OXIDE. (E.) Yoshida, T. H. (Nat. Inst. Genet., Mishima, Japan), T. Kuroki, Masuji and H. Sato. Gann 61(2):131-134, 1970.

Chromosomal changes were studied in the course of malignant transformation in vitro of 11 cultures of golden hamster embryonic cells by 4-nitroquinoline 1-oxide (4×10^{-5} and 5×10^{-5} M) and its derivative 4-hydroxyaminoquinoline 1-oxide (10^{-5} and 4×10^{-5} M). Results show chromosome

numbers with a tetraploid mode, a diploid mode (5/11 and 4/11 cell lines, resp.) and the remaining 2 having a bimodal distribution with a tetraploid and diploid peak. A hyperdiploid mode developed from a spontaneously transformed line. Chromosomal examination of cell lines at or before day 80 revealed 3 near-diploid and 1 near-tetraploid, while after 213 days 1 was near-diploid and 4 were near-tetraploid. Karyotypes of cell lines with diploid chromosomal numbers were different from normal cells (a large subtelocentric instead of submetacentric chromosome). Chromosomal transformation begins with gaps, breaks and deletions followed by heteroploid and polyploid karyotype changes due to nondisjunction and/or duplication of chromosome sets. It is concluded that among these cells, the more vigorous types may be selected and then malignant cell lines with altered karyotypes would be established.

70-1864 CHROMOSOME ABERRATIONS AND PERSISTENT NUCLEOLI OF YOSHIDA SARCOMA CELLS INDUCED BY 4-NITROQUINOLINE 1-OXIDE IN VITRO. (E.) Isaka, H. (Sasaki Inst., Chiyoda-ku, Tokyo). Gann 61(2):193-196, 1970.

A culture of cells taken from a Donryu rat bearing a 4-day-old Yoshida ascites sarcoma was inoc. with 4-nitroquinoline 1-oxide (NQO; 10^{-8} M, minimum growth inhibition conc.) and examined at 4-90 hours for chromosome aberrations and persistent nucleoli. Examination of treated metaphase cells revealed increased chromatid breakage and exchange compared to controls (10.6% and 16.6% for treated cells and 9.4% and 6.2% for controls). In carcinogen-treated cells the occurrence of chromatid breaks reached its highest level at 13 hours, then gradually decreased, compared to a peak at 30 hours for chromatid exchange (72- and 24-hour peaks, resp., for controls). Prominent nucleoli were present in treated cells in late prophase, prometaphase and metaphase cells within 30 hours; persistent nuclei were observed in metaphase cells at a 75% frequency in 24-hour specimens as compared to nearly unrecognizable ones in anaphase. It is likely that both the chromosomal and nucleolar abnormalities observed are also products of NQO-inhibited nucleic acid and/or protein synthesis of culture Yoshida sarcoma cells.

70-1865 CARCINOGENESIS IN TISSUE CULTURE. X. REJOINING OF SINGLE-STRAND BREAKS IN DNA OF MAMMALIAN CELLS INDUCED BY CHEMICAL CARCINOGENS (4-NITROQUINOLINE 1-OXIDE AND ITS DERIVATIVE IN VITRO. (E.) Horikawa, M. (Kanazawa U., Japan), O. Nikaide, T. Tanaka, H. Nagata and T. Sugahara. Exp. Cell Res. 59(1):147-152, 1970.

Ehrlich ascites tumor cells were cultured in a medium containing ^3H -thymidine and various conc. of 4-nitroquinoline 1-oxide (NQO) or 4-

hydroxyaminoquinoline 1-oxide (HAQO). Cells were collected and sedimentation analysis of DNA was performed, or the cells were processed for autoradiography. The NQO (conc. of 5×10^{-6} M to 1×10^{-5} M x 30 min.) and HAQO (1×10^{-4} M) induced single-strand breaks in DNA of cultured cells. A progressive shift of the sedimentation profile when cells were incubated after treatment suggests that Ehrlich ascites tumor cells can rejoin DNA fragments of previously damaged DNA. This was supported by autoradiographic evidence of DNA synthesis after NQO and HAQO treatment, although only slightly for the HAQO. It is concluded that the single-strand breaks are due to HAQO and, indirectly, due to the intracellular reduction of NQO to HAQO.

70-1866 BINDING OF ^{14}C -LABELED 4-NITROQUINOLINE 1-OXIDE TO DNA IN VIVO. (E.) Ikegami, S. (Nat. Cancer Ctr. Res. Inst., Chuo-ku, Tokyo), N. Nemoto, S. Sato and T. Sugimura. Chem. Biol. Interactions 1(4):321-330, 1969/70.

Adult male, strain ddN mice were inj. with Ehrlich ascites tumor cells (10^6 cells; i.p.), and after 7 days were inj. with ^{14}C -4-nitroquinoline 1-oxide (NQO; 20 μC in dimethyl sulfoxide and saline; i.p.). After 1 hour, ascitic fluid was collected and DNA extracted from the cells. Other mice were inj. with ^{14}C -4-NQO (5 μC ; i.p.) and DNA isolated for studies of binding time. DNA was also extracted from tumor cells of ^{32}P -inj. mice (0.1 mC; i.p.). Various procedures, including digestion, denaturation, density gradient centrifugation, enzymatic digestion and depurination, were performed on the DNA of ascites cells. Binding of radioactive NQO to DNA reached a max. at 4 hours and gradually decreased; RNA or proteins were not involved in this association. Transition of DNA from a double- to a single-stranded molecule was not affected by binding of NQO to DNA. Heat or alkaline denaturation did not cause release of label from DNA. After enzymatic digestion almost all radioactivity was released with the purine bases. It is concluded that the binding of NQO and its derivatives with the purine bases of DNA is covalent.

70-1867 ELECTRONIC STRUCTURES AND MECHANISM OF CARCINOGENICITY FOR ALKYLNITROSAMINES. (E.) Nagata, C. (Nat. Cancer Ctr. Res. Inst., Chuo-ku, Tokyo) and A. Imamura. Gann 61(2): 169-176, 1970.

In a physico-chemical study of the mechanism of carcinogenicity for alkyl nitrosamines, the electronic structures of methylethyl nitrosamine (a carcinogen) and diallyl nitrosamine (a non-carcinogen) and their hydroxylated compounds were studied and compared. The energy increment (ΔE) for each step in the metabolic conversion of alkyl nitrosamines and their non-carcinogenic analogs was calculated. The ΔE value for the

carcinogen was smaller than that for the non-carcinogen only for alkylation occurring through bimolecular nucleophilic substitution, and it is concluded that alkylation which proceeds via the $\text{S}_{\text{N}}2$ mechanism is the essential step for the carcinogenic action of alkyl nitrosamines.

70-1868 CARCINOGENIC ACTION OF DIMETHYL-NITROSAMINE IN TROUT NOT RELATED TO METHYLATION OF NUCLEIC ACIDS AND PROTEIN IN VIVO. (E.) Krüger, F. W. (German Cancer Res. Ctr. Inst. Exp. Toxicol. Chemother., Heidelberg), G. Walker and M. Wiessler. Experientia 26(5): 520-522, 1970.

Admin. of ^{14}C -dimethylnitrosamine (DMNA; 25 μC /0.84 mg, i.v., i.p. or i.m.) to adult homing pigeons, rainbow trout and frogs (*Rana esculenta*) showed ^{14}C -labeled DMNA incorporation in RNA of pigeon and frog liver. No DMNA incorporation was seen in RNA, DNA or protein of trout liver, either with varied dosage, inj. sites or time periods. It is concluded that no relationship exists between the carcinogenic and alkylating actions of DMNA in trout.

70-1869 THE EFFECT OF CHLORAMPHENICOL ON DIETHYLNITROSAMINE-INDUCED CARCINOGENESIS IN THE LIVER. (Ger.) Alonso, A. (U. Navarra Inst. Biol. Res., Pamplona, Spain) and G. Herranz. Naturwissenschaften 57(5):249, 1970.

Adult male Wistar rats were inj. i.p. either with chloramphenicol (C; 20 mg/kg x 2 days), diethylnitrosamine (DNA; 20 mg/kg x 2 days) or both compounds (alternating inj., same as above). Histological examinations were performed at different time intervals up to 80 days. The C-treated group showed no changes in the liver, while the DNA-treated group showed vacuolization of hepatocytes up to day 30, when changes characteristic of carcinogenesis occurred and hepatomas developed. No changes were seen for 25 days in the group treated with C+DNA; after that, a transient vacuolization and carcinogenesis (similar to the C-treated group) was seen and hepatomas developed. It is concluded that although chloramphenicol caused an inhibition of the initial toxic effect of DNA, it did not delay the induction of malignant hepatomas.

70-1870 STUDIES ON LUNG TUMOURS. I. METHYLATION OF DEOXYRIBONUCLEIC ACID AND TUMOUR FORMATION FOLLOWING ADMINISTRATION OF DIMETHYLNITROSAMINE TO MICE. (E.) Den Engelse, L. (Netherlands Cancer Inst., Amsterdam), P. A. J. Bentvelzen and P. Emmelot. Chem. Biol. Interactions 1(4):395-406, 1969/70.

Inbred, male 2-mo.-old C3Hf and GR mice were admin. dimethylnitrosamine (DMN; 10 ppm in the drinking water x 1 mo., then 1 ppm x 2 mo.). The GR mice were most sensitive to lung tumor

mation and the C3Hf mice developed more liver tumors. Other mice of both strains were admin. (7 and 10 mg/kg body wt., 1 admin./week x 13 wks, i.p.). Results for i.p. inj. were similar to those for DMN in the drinking water in relation to lung tumor induction; no conclusions on liver tumor formation can be made due to the short length of the experiment. Spontaneous lung tumor formation was also high for GR males, but as liver tumors were more frequent in C3Hf mice. No significant difference was seen in the inactive label in the 2 strains after a single i.p. inj. of ^{14}C -DMN; after 2 weeks, the 7-methylguanine content of the lung and liver DNA was 9% and 3%, resp. Results for the methylation process were decreased for liver and increased for lung and kidney when mice were pretreated with unlabeled DMN and then admin. the ^{14}C -DMN.

1871 ERYTHROPOIETIN ALTERATIONS IN THE PRESENCE OF DIMETHYLNITROSAMINE LIVER TUMORS IN CANINE AND SIMIAN SPECIES. (E.) Murphy, G. P. (Roswell Park Mem. Inst., Buffalo, N.Y.), E. A. Mirand, R. A. Steeves and E. C. Steeves. Invest. Urol. 7(4):283-289, 1970.

Male and female rhesus monkeys and adult mongrel dogs were admin. dimethylnitrosamine (DMN; 25 mg/kg, single dose). For 34 weeks, various chemical tests were performed including erythropoietin stimulating factor (ESF) assays in plasma. For dogs, acute liver necrosis was observed, but renal function was greatly impaired, in comparison to monkeys. Renal or hepatic tumors were not found in dogs for 34 weeks or at autopsy; in monkeys, liver tumors were not observed and no renal tumors were found. Increase in plasma ESF levels was greater for dogs than monkeys (9.23- and 4.5-fold increase, resp., in the absence of anemia). Unlike human primates, the dog has no extrarenal erythropoietin activity and increased ESF levels are attributed directly to renal damage. As no tumors developed, they are not considered a consequence of ESF elevation; although, in the monkey, increased ESF is attributed to liver damage.

1872 THE REACTION OF N-METHYL-N'-NITRO-N-NITROSOGUANIDINE WITH DNA IN THE INTACT CELL. (E.) Craddock, V. M. (Med. Res. Council, Carshalton, Surrey, England). Chem. Biol. Interactions 1(2):234-237, 1969/70.

Male Wistar albino rats were inj. with ^{14}C -N-methyl-N'-nitro-N-nitrosoguanidine (NG; 3 mg/ml water, 5 doses of 5 ml x 1 hour by stomach tube). Analysis of liver and stomach (and small intestine) tissue showed no radioactivity in the 7-methylguanine of DNA. Results are similar to those for kidney DNA after treatment with dimethylnitrosamine or N-methyl-N-nitrosourea. It is suggested that the methylation process is relevant in carcinogenesis due to NG and related compounds.

70-1873 SEQUENTIAL MORPHOLOGICAL CHANGES IN N-METHYL-N'-NITRO-N-NITROSOGUANIDINE CARCINOGENESIS IN THE GLANDULAR STOMACH OF RATS. (E.) Saito, T. (Kyushu U. Med. Sch., Fukuoka, Japan), K. Inokuchi, S. Takayama and T. Sugimura. J. Nat. Cancer Inst. 44(4):769-783, 1970.

Male 8-week-old Wistar rats were admin. N-methyl-N'-nitro-N-nitrosoguanidine (MNG; 167 $\mu\text{g}/\text{ml}$ drinking water x 40 weeks, then 83 $\mu\text{g}/\text{ml}$). Examination of the stomach from day 1 to about 60 weeks after MNG admin. showed 3 stages of glandular proliferation of the stomach. To week 20, atrophy and erosion of mucosa and regenerative hyperplasia were evident. Stage 2 (weeks 20-30) involved adenomatous hyperplasia. Adenocarcinomas were evident with invasion of submucosa, muscularis propria and serosa from week 30 on. Almost all rats had adenocarcinoma with serosal invasion after 60 weeks. No relationship between intestinal metaplasia and MNG-induced stomach cancer was observed.

70-1874 TUMOR PRODUCTION IN THE GLANDULAR STOMACH AND ALIMENTARY TRACT OF THE RAT BY N-METHYL-N'-NITRO-N-NITROSOGUANIDINE. (E.) Sugimura, T. (Nat. Cancer Ctr. Res. Inst., Chuo-ku, Tokyo), S. Fujimura and T. Baba. Cancer Res. 30(2):455-465, 1970.

Male 6-week-old Wistar rats were admin. N-methyl-N'-nitro-N-nitrosoguanidine (33 or 38 $\mu\text{g}/\text{ml}$ in the drinking water x 6 mo., increased to 83 and 167 $\mu\text{g}/\text{ml}$, resp., from mo. 7 until the end of the experiment). The av. body wt. of the treated rats was similar to that of controls up to 120 days, and then was less; no leukopenia occurred up to 120 days; and by 11 mo., many of the animals in the high conc. group had died, while most of the low conc. group and the controls were still alive. Tumors of the glandular stomach were found in 14/16 rats, with no significant difference between the 2 experimental groups in frequency and type of tumor.

70-1875 ADENOCARCINOMA OF GLANDULAR STOMACH AND DUODENUM IN WISTAR RATS INGESTING N-METHYL-N'-NITRO-N-NITROSOGUANIDINE, HISTOPATHOLOGY AND ASSOCIATED SECRETORY CHANGES. (E.) Bralow, S. P. (Jefferson U. Med. Coll., Philadelphia, Pa.), M. Gruenstein, D. R. Meranze, A. Bonakdarpour and M. B. Shimkin. Cancer Res. 30(5):1215-1222, 1970.

Male Wistar rats, about 6 weeks old, were admin. N-methyl-N'-nitro-N-nitrosoguanidine (NG; 83 mg/liter, in the drinking water x 25 or 52 weeks). NG was not toxic, but a significant difference was seen in drinking water consumption between the treated and control rats (21 and 26 ml/day, resp.). To week 39, wt. loss was due to lung infection, after that it was due to tumor formation. Tumors developed in 5/10 (50%) and 38/54 (70%) rats treated 25 and 52 weeks, resp. Separate groups of rats admin. NG (after 3 days

or 28, 41 and 52 weeks) were subjected to 4-hour pyloric ligation in a study of gastric secretion. Pepsin secretion increased significantly after 3 days or 28 weeks, with no other differences from controls. Despite abnormal histology, atrophy and tumor formation by 52 weeks of NG treatment, gastric secretion vol. and acid conc. were reduced, and pepsin secretion was at control levels. It is suggested that NG treatment (which is carcinogenic, but not toxic) be used to study suspected foods and induction of stomach cancer as well as the effects of antimetabolites.

70-1876 TRANSPLACENTAL CARCINOGENIC EFFECT OF N-NITROSOMETHYLUREA IN RATS. (Rus.)

Aleksandrov, V. A. (N. N. Petrov Sci. Res. Inst. Oncol., Leningrad, USSR). Vop. Onkol. 15(4): 55-61, 1969.

Female, random-bred rats were admin. N-nitrosomethylurea (NMU; 20 mg/kg, single i.p. inj. on day 21 after insemination); 82 offspring of 12 rats not treated with NMU and 19 non-pregnant female rats treated with NMU (dosage as above) served as controls. Mortality of newborn rats from the experimental group, 1 week after birth, was slight (20.4%) and similar to that of controls (10-16%), while in rats up to 5 mo. old it increased to 23.3%. Most of the dead rats showed signs of intercurrent diseases. Offspring of NMU-treated rats exhibited delayed postnatal development when compared to controls. Some showed pronounced body tremor and discoordination gait at age 3-5 mo. One female offspring had congenital cataracts of both eyes. Of the offspring of NMU-treated rats, 43/54 (79.6%; 15 females, 28 males) survived for 8 weeks after birth; 33/54 (76.7%; 11 females, 22 males) were alive at the time of appearance of first tumor; and 13/54 (39.4%; 3 females, 10 males) developed tumors. Kidney tumors (all adenomas) developed in 6 males; brain tumor (astroblastoma) was found in 1 male; spinal cord tumors (1 spongioblastoma, 1 ependymoblastoma) developed in 2 males; trigeminal nerve tumors developed in 2 males and 1 female; generalized reticulosis occurred in 1 male; there was reticulosarcoma of the large intestine in 1 female; and anterior mediastinal tumor developed in 1 female. Mammary carcinoma with cylindromatous structures developed in 1/6 NMU-treated female rats 395 days after treatment. Hyperplasia of mucosa and single papillomas of the forestomach were found in 2/19 rats which died 1 yr. after treatment. No tumors were detected in the control offspring that survived more than 500 days.

70-1877 EARLY STAGES OF TUMOURS OF THE CENTRAL NERVOUS SYSTEM. MORPHOLOGIC STUDIES OF EXPERIMENTALLY-INDUCED TUMORS. (Ger.)

Jänisch, W. (Erfurt Med. Acad. Path. Inst., Germany), D. Schreiber, R. Warzok and G. Osske. Exp. Path. 4(1):60-68, 1970.

i.v. inj. of methylnitrosourea induced tumors of the central nervous system in 50.7% and 66.7% of the treated rats and rabbits, resp. In rats, i.p. inj. induced similar tumors in 56.8%; intragastric admin. induced tumors in 14.7%. Intracerebral tumors predominated by about 7:1. In the case of gliomas, tumor development began with proliferation of oligodendroglial cells which were histologically indistinguishable from normal cells of the same type. Later, relatively large, diffuse masses of oligodendroglial cells formed, with an increased frequency of atypical cells showing enlarged and irregular, chromatin-rich nuclei. Polynuclear giant cells appeared, gradually dominating the picture. Intracerebral sarcomas arose from blood vessels, with 1 form beginning with a characteristic inflammatory process of the adventitia, the other with marked cellular proliferation in the walls of small vessels, accompanied by extension of small groups of malignant cells to invade neighboring tissues. Both forms of sarcomatous development were frequently found in the same animal.

70-1878 THE ULTRASTRUCTURE OF EXPERIMENTALLY INDUCED CEREBRAL TUMORS IN RABBITS.

(Ger.) Schreiber, D. (Erfurt Med. Acad. Path. Inst., Germany), A. Lageman, W. Jänisch and W. Dietz. Exp. Path. 4(1):6-15, 1970.

Multiform glioblastomas induced in 3/5 rabbits treated by i.v. inj. of methylnitrosourea in buffered saline showed large, deeply invaginated, polymorphous nuclei with osmiophilic nuclear content concentrated at the nuclear membrane. The cytoplasm contained a rough endoplasmic reticulum and was rich in ribosomes, which clustered into small complexes. It also contained microtubules and osmiophilic bodies with clearly defined membranes. Intracerebral sarcomas induced by the same treatment in 2/5 animals also showed a rough endoplasmic reticulum, with numerous cisternae containing a fine, granular substance. Nuclei were elongated and profoundly invaginated; they contained multiple, very large nucleoli and deposits of rough granules in the karyoplasm which resembled ribosomal material. The cells had highly irregular walls, with numerous, narrow pseudopodia which appeared to mesh with invaginations in the walls of neighboring cells. No collagenous fibers were apparent.

70-1879 METHYLNITROSOUREA-INDUCED MALFORMATIONS OF BRAIN IN SD-JCL RATS. (E.) Koyama,

T. (Kyoto U. Med. Sch., Japan), J. Handa, H. Handa and S. Matsumoto. Arch. Neurol. (Chicago) 22(4):342-347, 1970.

Pregnant rats were inj. with N-methyl-N-nitrosourea (MNU; single admin. of 10, 20 or 40 mg/kg on days 8.5-15.5 of gestation, i.p.) and the embryos (1023) were studied on day 20. Inj. of 40 mg before day 11.5 was fatal to all embryos

20 mg, 100% mortality occurred when rats were fed on day 9.5, and 72.2% mortality was seen at 10 mg admin. at that time. Rat embryos were most sensitive on day 12.5; with 100% malformations for all dosages. External malformations (age-specific) included microcephalus, syndactylia, hypoplasia of cerebral structures, facial defects, micrognathia, dislocation and retardation of growth. By day 15.5, MNU had no teratogenic effect on rat embryos. From day 11.5, a parallelism between external malformations and central nervous system involvement was seen, which returned to near normal on day 15.5. Continued inhibitory effects of MNU were seen in the form of ataxia, tremor and retarded growth of offspring of rats treated as late as day 20.5 gestation.

1880 EXPERIMENTAL TUMORS INDUCED IN RATS BY ADMINISTRATION OF DERIVATIVES OF N-NITROSO-N-ETHYLUREA. I. MORPHOLOGICAL AND HISTOCHEMICAL OBSERVATIONS. (It.) Schiffer, D. (U. Turin, Psychiat. Clin., Italy), A. Fabiani, E. Grossi-Paoletti and P. Paoletti. Acta Neurol. (Napoli) 24(4):561-562, 1969.

Male, pregnant Long Evans rats were inj. with N-nitroso-N-ethylurea (NEU; 10 mg/kg, i.v.) and 10-month-old, male Long Evans rats were admin. N-nitroso-N-methylurea (NMU; 25 mg/kg, i.v.). Tumors developed after 6-10 mo. in 21 offspring of the NEU-treated rats (13 spinal neurinomas, 5 in the Gasserian ganglion, 1 with multiple ependymomas of the spine). Tumors were perivascular, with no characteristics of adjacent nervous tissue; granules were positive to phosphoric acid and tumors showed non-specific resistance to esterases and β -glucuronidase. NEU-treated rats developed external gliomas (3/39 intracranial, 6/39 medullary and 11/39 multiple) which resembled human malignant ependymogliomas or glioblastomas with high activity of lysosomal hydrolytic enzymes.

1881 EXPERIMENTAL TUMORS INDUCED IN RATS BY ADMINISTRATION OF DERIVATIVES OF N-NITROSO-N-ETHYLUREA. II. OBSERVATIONS ON THE COMPOSITION OF STEROLS. (It.) Grossi-Paoletti, E. (U. Turin, Inst. Pharmacol. Clin. Neurosurg., Italy), P. Paoletti, D. Schiffer and A. Fabiani. Acta Neurol. (Napoli) 24(4):563-564, 1969.

The desmosterol (D) content in all of the various tumors induced by N-nitroso-N-ethylurea and N-nitroso-N-methylurea in Long Evans rats was about 16% of the total steroid content. D or other cholesterol derivatives could not be demonstrated in noninfiltrated cerebral or medullary tissue adjacent to the tumors. It is concluded that D content is not indicative of the tumorigenic nature of the tissue, but rather its maturity and undifferentiation.

70-1882 INDUCTION OF MALIGNANT TUMORS IN RATS BY ORAL ADMINISTRATION OF N,N'-DIMETHYLUREA AND SODIUM NITRITE. (Ger.) Sander, J. (U. Tubingen Inst. Hyg., Germany). Arzneimittelforschung 20(3):418-419, 1970.

Female rats of the SIV-50, Ivanova or Kissleg strains (120 g) were admin. dimethylurea (DMU; 0.1% or 0.3% in the drinking water) and sodium nitrite (NaN; 0.3% in the feed), both for 56 days. All animals developed malignant tumors (unspecified) of the heart, thymus, kidneys and/or thyroid before they died 117-432 days after discontinuing treatment. Increasing the DMU content of the water to 0.9% resulted in rejection by the animals, and all died without tumors within 4 weeks. No tumors developed in animals admin. 0.3% DMU in the water + normal feed or in animals admin. feed with 0.3% NaN+ untreated drinking water.

70-1883 CARCINOGENIC EFFECT OF N,N'-DINITROSOPIPERAZINE IN MICE. (Rus.) Zabezhinskii, M. A. (N. N. Petrov Sci. Res. Inst. Oncol., Leningrad, USSR). Vop. Onkol. 15(6):104-106, 1969.

Admin. of N,N'-dinitrosopiperazine (DNP; 10 and 50 mg/kg/week until death, s.c. or 20 mg/kg, 6 admin./week until death, p.o.) to CC57W mice induced development of tumors in 306-509 days. For the 10, 50 and 20 mg doses, the number of mice with tumors was 14/50, 20/50 and 17/50, resp. (28%-40%). Liver tumors (adenomas, hemangiomas, carcinomas or reticulum cell sarcomas) developed predominantly in the 50-mg dose group (3, 3, 1 and 1, resp.). Frequency of lung tumors was similar. DNP caused nose bleeding, hyperemia, edema, alveolar hemorrhage and inflammation of the lungs, and necrosis, hyperplasia, parenchymatous dystrophy and initial cirrhosis of the liver. Other effects in individual mice included hemangiomas, serous ovarian cysts, lung adenocarcinoma, liver hemangioma, bladder papilloma, spindle cell sarcoma in the nasal region and a spontaneous cutaneous papilloma.

70-1884 BASIC CYTOPATHOLOGIC DIFFERENCES IN THE GENESIS OF CIRRHOSIS OF THE LIVER AND LIVER-CELL CARCINOMA. (Ger.) Bannasch, P. (U. Wurzburg Path. Inst., Germany). Verh. Deutsch. Ges. Path. 53:335-341, 1969.

In rats of an unspecified strain which received drinking water containing 12 or 20 mg% N-nitrosomorpholine, central hepatic parenchymal lesions, primarily of the acinus cells, involved the disappearance of glycogen from the cells, disorganization of the ergastoplasm and resultant coagulation necrosis and widespread cirrhotic degeneration. These changes were

accompanied by a massive increase of glycogen content in peripheral acinus cells, which also showed dislocation (as contrasted to disorganization) and reduction of the ergastoplasm, progressive hypertrophy of agranular endoplasmic reticulum and the appearance of large, glycogen-filled vacuoles. Progressive reduction of the increased glycogen levels was accompanied by a sharp increase of ribosomal conc., transitory fatty infiltration of the cytoplasm, and transformation of agranular into granular endoplasmic reticulum. It is concluded that the 2 processes are essentially independent reactions to the presence of the toxic substance, with no causal or sequential relationship between them.

70-1885 HISTOCHEMICAL STUDIES ON RAT LIVER PROTEINS DURING 4-DIMETHYLAMINOAZOBENZENE CARCINOGENESIS. (E.) Brière, N. (U. Sherbrooke, Quebec, Canada) and R. Daoust. Cancer Res. 30(5):1370-1375, 1970.

Male albino Wistar rats (200-220 g) were fed 4-dimethylaminoazobenzene (DAB; 0.06% soln. in the diet x 180 days). Groups of 10 animals were sacrificed at 30-day intervals; 4/10 were inj. with ^3H -leucine (1 $\mu\text{C/g}$ body wt.) 1 hour prior to sacrifice. Histological examination and autoradiography of the livers and other organs were performed. Prolonged DAB feeding resulted in a marked decrease in staining of cytoplasmic proteins during formation of hyperbasophilic foci and hepatomas. Extraction of nucleic acids from livers of DAB-fed rats showed the same enhancement of protein staining as for normal livers. At early stages of DAB admin., a slight decrease in label of nuclear protein occurred, with increases after formation of hyperbasophilic foci and hepatoma development. It is concluded that DAB slightly lowers amino acid incorporation into liver protein, but intensity of label remains constant during DAB feeding and the consequent development of hepatomas. It is suggested that some unusual form of RNA binds to and masks cytoplasmic proteins during neoplastic transformation.

70-1886 HISTOCHEMICAL AND HISTOCHROMATOGRAPHIC DATA ON THE DYNAMICS OF LIPID METABOLISM IN EXPERIMENTAL HEPATOMA IN RATS. (Rum.) Stănilă-Oană, L. Clujul Med. 42(4):527-535, 1969.

Male white rats were admin. 4-dimethylaminoazobenzene (10 mg/day x 15-120 days) and their livers examined histochemically and histochematographically. Hepatomas developed in 90-105 days. Before development of tumors, especially from days 60-90, liver content of neutral fats increased, and lipase activity markedly decreased and was absent in connective tissue. It is suggested that the decrease in phospholipids (lecithin and cephalin) after tumor development was due to reduced oxidative phosphorylation.

70-1887 MITOTIC RESPONSES TO PARTIAL HEPATECTOMY IN PRENEOPLASTIC RAT LIVER. (E.) Hughes, P. E. (Baker Med. Res. Inst., Prahran, Victoria, Australia). Chem. Biol. Interactions 1(3):315-320, 1969/70.

Adult, male hooded Wistar rats were fed 3'-methyl-4-dimethylaminoazobenzene (3-MeDAB; 0.06% in the diet x 2 or 5 weeks) or 2-methyl-4-dimethylaminoazobenzene (2-MeDAB, as above) and then subjected to either 1 or 2 partial hepatectomies. Mitotic responses of regenerating rat liver (onset, duration and magnitude) were similar for 1 or 2 partial hepatectomies. A comparison of 3-MeDAB admin. for either 2 or 5 weeks, showed a delayed mitotic response for the rats fed 5 weeks. For 3-MeDAB, a proliferative response occurred after 4 weeks.

70-1888 LIVER CELL RESPONSES TO THE CARCINOGEN 3'-METHYL-4-DIMETHYLAMINOAZOBENZENE. (E.) Hughes, P. E. (Baker Med. Res. Inst., Prahran, Victoria, Australia). Chem. Biol. Interactions 1(3):301-305, 1969/70.

Male hooded Wistar rats (160-190 g) were admin. 3'-methyl-4-dimethylaminoazobenzene (MeDAB; 0.06% in the diet x 1-6 weeks). Tumors of the liver developed in no rats fed MeDAB for 3 weeks and in 22/32 (69%) fed 5 weeks or more. Proliferative changes and the proportion of parenchymal cells increased after 5 weeks. It is concluded that MeDAB must be admin. during the period of proliferative response for high frequency of tumor induction to occur. No tumors were induced when admin. of MeDAB was ended after peak binding to protein.

70-1889 CARCINOGENICITY AND TARGET ORGANS OF METHOXYL DERIVATIVES OF 4-AMINOAZOBENZENE IN RATS. II. EFFECT OF VARIOUS CONCENTRATIONS OF 3-METHOXY- AND 2,5-DIMETHOXY-4-AMINOAZOBENZENE IN THE DIET. (E.) Odashima, S. (Sasaki Inst., Chiyoda-ku, Tokyo) and Y. Hashimoto. Gann 61(2):153-160, 1970.

Male Donryu rats were fed a diet containing 0.025%, 0.04% or 0.09% 3-methoxy-4-aminoazobenzene (MeOAB) or 2,5-dimethoxy-4-aminoazobenzene (MeO₂AB). Liver tumors developed in most rats fed MeOAB, and more extrahepatic tumors occurred in those fed the higher dose. Among 26 animals receiving 0.09% MeOAB, tumors of the spleen and ear duct developed in 3, and tumors of skin and small intestine in 2. At lower conc. of MeOAB, only 2/46 animals developed splenic tumors. MeO₂AB at 0.09% was very toxic, and all rats died during week 3. All animals receiving the lower conc. of MeO₂AB sustained severe damage of the testicular tubules characterized by necrosis, deposition of calcium and arrest of spermatogenesis. Adrenal medullary adenoma developed in 2 rats receiving 0.04% MeO₂AB.

1890 A STUDY OF THE CARCINOGENICITY OF A SERIES OF STRUCTURALLY RELATED 4-METHYLAMINOAZOBENZENES. (E.) Bebawi, G. M., S. Kim and J. P. Lambooy (U. Maryland Coll., Baltimore). Cancer Res. 30(5):1520-1524, 1970.

Female Sprague-Dawley rats (125-150 g) were fed various 3',4'-disubstituted-4'-dimethylaminoazobenzenes (DAB; 7 admin./week x 50-365 days). All DAB derivatives were carcinogenic if fed 365 days. Comparison of their potency in relation to the 3' and 4' positions revealed an additive effect of combinations of these substituents. Male CFE rats (100-200 g) were admin. the DAB derivatives (1 mg/kg body wt. in corn oil, single dose i.p.). The presence of an ethyl group at the 3' and 4' sites of the 10 compounds accentuated DAB binding to liver protein (though not exceptionally if both have ethyl groups) and a chloro group lessened it; chloro groups prevented it. It is concluded that liver protein binding and carcinogenicity of disubstituted DAB compounds are only generally related.

1891 SURVEY OF THE LINKAGE BETWEEN CARCINOGENIC NITROGENOUS COMPOUNDS AND LIVER PROTEINS DURING HEPATIC CARCINOGENESIS. (E.) Prodi, G. (U. Bologna Inst. Gen. Path., Italy), C. Finzi and A. T. Di Marco. Boll. Soc. Biol. Sper. 45(1):21-24, 1969.

Male rats were admin. 3'-methyl-4-dimethylaminoazobenzene (MeDAB; 0.04% or 0.06% in the diet x 7 mo.) in order to test for the "deletion" of a stable union of a nitrogenous carcinogen to liver protein. Various neoplastic lesions developed and a slight decrease in protein-carcinogen compound occurred at 4 mo. with 0.06% MeDAB. Results for 0.04% MeDAB, and at times earlier than 4 mo. for 0.06% MeDAB, were highly variable. It is concluded that there is no relationship between liver protein-carcinogen binding and the frequency of neoplasms.

1892 BINDING OF 3'-METHYL-p-DIMETHYLAMINO-AZOBENZENE AND DNA IN DIFFERENT ORGANS IN THE REGENERATING LIVER OF RATS. (It.) Prodi, G. (U. Bologna Inst. Gen. Path., Italy), C. Finzi and C. Franceschi. Boll. Soc. Ital. Biol. Sper. 45(1):24-26, 1969.

Female, adult Wistar rats were admin. ³H-3'-methyl-4-dimethylaminoazobenzene (95 mC/mole; 2 mC/mole olive oil, i.p.). In unoperated animals after 48 hours, the DNA specific activity in liver was 10-fold that for lung or spleen and 3.5-fold that for kidney. Regenerating liver had a DNA-specific activity about twice that of normal liver.

1893 ALTERATION OF THE RNA/DNA RATIO OF RAT LIVER ASSOCIATED WITH THE PREVENTION

OF AZO DYE CARCINOGENESIS BY DIETARY CHLORAMPHENICOL. (E.) Blunck, J. M. (U. Melbourne, Victoria, Australia). Life Sci. 9, Pt. 2(1): 51-59, 1970.

Groups of 22-25 adult male Sprague-Dawley rats were fed diets containing 2% chloramphenicol or 3'-methyl-4-dimethylaminoazobenzene (MeDAB; 0.06%) or both for 12 weeks; the short-term effects of this diet on rat livers were investigated using young (100-150 g) pair-fed Sprague-Dawley rats. The incidence of hepatoma and cholangioma induced by MeDAB was significantly reduced by simultaneous feeding with chloramphenicol. In rats given either compound, and especially with both compounds, there was a significant increase in the liver wet wt./100 g body wt. as compared to controls. No significant difference in the RNA/DNA ratio was found in the liver of rats fed both compounds and in those of controls, but chronic chloramphenicol feeding increased the ratio; also, the phase distribution of mitotic figures in the liver of rats receiving both compounds was closer to that of partially hepatectomized animals than that of MeDAB-treated rats. No significant alteration in hepatic protein-bound dye levels was found up to 10 days.

70-1894 LIVER AND LUNG TUMORS INDUCED BY 3,3'-DICHLORO-4,4'-DIAMINODIPHENYLMETHANE IN RATS. (Ger.) Grundmann, E. (Bayer AG Dye Co. Inst. Exp. Path., Wuppertal-Elberfeld, Germany) and D. Steinhoff. Z. Krebsforsch. 74(1):28-39, 1970.

Admin. of 3,3'-dichloro-4,4'-diaminodiphenylmethane (0.1% in a protein-deficient diet; total dose, 27 g/kg x 500 days) to 100-day-old Wistar II rats induced malignant tumors in 23/25 males (22 hepatomas with metastases to the lung in 2 and to the brain in 1, and 7 with primary lung tumors) and 20/25 females (18 hepatomas, 3 also with primary lung tumors). Of the controls, 2/50 developed tumors (mammary fibroadenomas). The av. survival period from start of experiment was 565 days for males, 535 days for females and 730 days for controls. It is concluded that although the compound is less toxic (10/10 rats survived a single p.o. or s.c. dose of 5000 mg/kg) than 4,4'-diaminodiphenylmethane, it is a more potent carcinogen.

70-1895 STUDIES ON MORPHOLOGICAL PRECURSORS OF THE MOUSE HEPATOMA INDUCED WITH o-AMINOAZOTOLUENE. II. SEQUENCE TO THE DEVELOPMENT OF HEPATOMA AND ITS GRADATION IN STRAIN SL MICE. (E.) Itoh, K. (Mie Prefect. U. Sch. Med., Tsu, Japan). Mie Med. J. 29(2):173-187, 1969.

Female, inbred virgin SL mice (27-49 days old) admin. o-aminoazotoluene (o-AT; 10 mg/0.1 ml olive oil; 1 s.c. inj./mo.) were generally more susceptible to induction of tumors of the liver

than males. Liver tumors developed earlier in o-AT-treated progeny of these mice, but only in the males. The gradual transformation of normal liver cells into tumor form is described. No increased frequency or sex differences were seen for o-AT-induced leukemia, but lung neoplasms did increase. Amyloidosis, hemangioendothelioma, a mammary tumor and other lesions are also described.

70-1896 ELECTRON MICROSCOPIC STUDY OF METHYLCHOLANTHRENE-INDUCED EPIDERMAL CARCINOGENESIS IN MICE: MITOCHONDRIAL DENSE BODIES AND INTRACISTERNAL A-PARTICLES. (E.) Kakefuda, T. (NCI, Bethesda, Md.), E. Roberts and V. Sontzeff. Cancer Res. 30(4):1011-1019, 1970.

Mice were painted with 3-methylcholanthrene (MC; 0.6% in benzene, 3 admin./week x 3 mo.) or benzene alone, and epidermal changes were studied by electron microscopy. Papillomas induced by MC had numerous intramitochondrial dense bodies; these did not seem to have a specific relationship to carcinogenesis, but may have been related to intracellular keratinization and/or keratin synthesis. Large amounts of intracisternal A-particles were found in MC-induced squamous cell carcinomas, but they were not oncogenic themselves. When cell-free particulates from squamous cell tumors were inj. into newborn mice, tumors developed in 16/31; 15/16 were mammary carcinomas and 1/16 was a lymphocytic leukemia. These contained a mixture of Type A, B and C particles, but they did not resemble the intracisternal A-particles found in the original squamous cell carcinoma cells. Changes in arginase activity observed during epidermal carcinogenesis were given only a correlative association with malignant transformation.

70-1897 FINE STRUCTURE OF NUCLEAR INCLUSIONS IN MURINE PULMONARY TUMOR CELLS. (E.) Flaks, B. (U. Bristol Med. Sch., England) and A. Flaks. Cancer Res. 30(5):1437-1443, 1970.

Lung tissue from BALB/c mice was maintained in culture with 3-methylcholanthrene (4 µg/ml x 1-6 days) and implanted s.c. into isologous mice. Resultant adenomas and adenocarcinomas were transplanted serially. Electron microscopic study of cellular fine structure revealed 3 types of nuclear inclusions in the pulmonary tumors: 1) double-membraned with cytoplasmic material, 2) double-membraned with membranous tubules, free ribosomes and lipid granules, and 3) single-membraned with large dense bodies and granular material. It is suggested that the abnormal presence of nuclear inclusions and membranous tubules in pulmonary tumor cells indicates some specific function of these structures in neoplasia.

70-1898 MULTIPLE MAMMARY TUMORS IN RATS AFTER INTRAGASTRIC INTRODUCTION OF CARCINOGENIC SUBSTANCES. (Jap.) Mercker, P. C. (Columbia U. Coll. Pharm., New York, N. Y.). Ochanomizu Igaku Zasshi (Ochanomizu Med. J.) 16(3):35-45, 1968.

In 300 Sprague-Dawley rats admin. 3-methylcholanthrene (MC; 10 mg, 3 admin./week, total dose 210 mg), MC (single 100 mg dose) and 7,12-dimethylbenzanthracene (DMBA; single 15 mg dose, all by stomach intubation), tumors appeared in 5-10 weeks. The frequency of tumors increased by week 17, then leveled off. The groups receiving multiple MC infusions showed highest frequency of tumors (88%), followed by the DMBA group (71%) and the MC group (29%). The tumors were multiple in areas of the neck, axilla, stomach and groin. Mammary tumors accounted for 94% of all tumors. Most of the tumors were papillary or papillotubular adenocarcinomas. In 6 cases, tumor regressed when food intake was restricted, and increased when the restriction was removed. The effect of autoimmunization with ablated tumors (homogenized with Freund adjuvant) was studied. Tumor growth and tumor frequency were inhibited more in these animals than in those in which only adjuvant was used (same conditions, 4 weeks after surgery). Tumors greater than 3 cm in size showed a high growth rate when recurring. In animals admin. testosterone propionate (5 mg/day x 5 weeks), 70-80% of the tumors regressed, as in oophorectomized rats. The WBC count increased with appearance of tumors, continued as the tumors developed and then decreased. Hematocrit decreased with the growth of tumors.

1899 EXPERIMENTAL CANCER INDUCTION IN GUINEA PIGS BY HEATED AND NON-HEATED FATS IN COMBINATION WITH METHYLCHOLANTHRENE. (Ger.) Zaldívar, R. (85 W. Northfield Rd., Livingston, N. J.). Arch. Hyg. Bakt. 153(3): 211-219, 1969.

A total of 144 female guinea pigs (440 g wt., undetermined strain) were inj. with unheated fat (from the peritoneal cavity of normal guinea pigs), preheated fat (361-365° x 30 min.), unheated fat + 0.9 mg 3-methylcholanthrene (MC) or preheated fat + 0.9 mg MC (all 0.05 or 0.10 ml into the wall of the stomach). Animals were examined for histopathological changes from days 16-240. The animals treated with unheated fat showed only local nonspecific inflammatory changes, whereas proliferating gastric lesions were found in 18/36 (50%) treated with preheated fat, 19/40 (47.5%) treated with unheated fat + MC and 19/39 (48.7%) of the group treated with preheated fat + MC. Infiltration into the submucosa or muscularis propria was seen in 0%, 38.8%, 37.5% and 38.4%, resp. Atypical morphological changes of basal glands of the deep mucosa were also seen in the 3 affected groups.

1900 SPECIALIZED INTERCELLULAR JUNCTIONS IN TUMOR CELLS - AN ELECTRON MICROSCOPE STUDY OF MOUSE SARCOMA CELLS. (E.) Clarke, A. (U. Washington Sch. Med., Seattle). *Anat.* 166(2):199-201, 1970.

Implantation of 3-methylcholanthrene (MC; s.c.) in BALB/c, C57BL and C3H mice produced tumors in 100%. Electron microscopic examination of sarcoma cells showed them to be closely-arranged in 2 types of specialized junctions: 1) the tight junction which controls passage of substances through intercellular spaces and 2) the intermediate junction and desmosome which are binding sites to support structural integrity of tissues. A specialized structural differentiation of MC-induced sarcomas is suggested.

1901 THE INDUCTION OF MALIGNANT TUMORS IN THE UTERUS OF MICE BY 20-METHYLCHOLANTHRENE AND THE EFFECT OF SIMULTANEOUS ESTROGEN TREATMENT ON HISTOLOGICAL STRUCTURE AND GROWTH RATES OF TUMORS. (Ger.) Boquai, E. (U. Berlin Gynec. Clin., Germany), H. Ebner and W. Sandritter. *Z. Krebsforsch.* 74(1):59-75, 1970.

Female NMRI mice (25-30 g) were admin. 17α -hydroxyprogesterone (OHNP; $2 \times 200 \mu\text{g}$, 3 days i.p., s.c.), either 6 days before, or 6 days after, intrauterine implantation of 3-methylcholanthrene (MC; 2.5 mg) and the treatment continued until death of the animals. Malignant tumors of the uterus developed in 22/30 (73.3%) of mice treated with MC alone, in 13/20 (65%) treated 6 days before with OHNP and then MC, and in 7/10 (70%) treated with OHNP 5 days after MC-implantation. The mean induction time was 18.3, 26.1 and 17.2 weeks, resp., indicating a significant delay in tumor development for the OHNP-pre-treated group. Tumors were about 70% squamous cell carcinomas, about 30% sarcomas and a few adenocarcinomas. The OHNP-treated animals frequently showed keratinization, indicating that hormone treatment affected degree of differentiation; this is considered a criterion of gestagen treatment. No clear-cut relationship between tumor type and its DNA distribution could be demonstrated.

1902 GLUCURONYLTRANSFERASE ACTIVITY IN TRANSPLANTABLE RAT HEPATOMAS. (E.) Wiersma, K. K. (NCI, Bethesda, Md.), H. M. Dyer, J. L. Thompson and E. L. Kuff. *Cancer Res.* 30(2):274-279, 1970.

Various hepatomas were implanted into Buffalo, C3H/He and male Holtzman rats and the p-nitrobenzyl glucuronyltransferase activity measured. The enzyme level was high in well-differentiated Morris hepatomas (7794A, 7787 and 7316A) and in the H35 and H139 hepatomas, but was comparable to normal and host liver in the undifferentiated H35 and 3924A and 3683 hepatomas and in the high-

and low-catalase hepatomas. Glucuronyltransferase was detected in the Novikoff hepatomas, but the levels were unreliable. Microsomes from the well-differentiated tumors showed an increase in the number of enzymatic sites per unit of microsomal protein as compared to liver. Hepatomas of male Holtzman rats given 3-methylcholanthrene (5 mg/100 g body wt.) had an enzyme activity similar to that in H35, H139 and 7794A hepatomas after 45 hours.

70-1903 PHARMACOLOGIC INDUCTION OF SERUM HEMOPEXIN BY 3-METHYLCHOLANTHRENE AND ALLYLISOPROPYLACETAMIDE. (E.) Ross, J. D. (Scripps Clin. Res. Found., La Jolla, Calif.) and U. Muller-Eberhard. *J. Lab. Clin. Med.* 75(4):694-702, 1970.

Admin. of 3-methylcholanthrene (MC; 4 mg/kg/day in corn oil, i.p.) and allylisopropylacetamide (AIA; 400 mg/kg/day in saline, s.c.) to adult male New Zealand white rabbits significantly increased levels of serum hemopexin (Hx) in a pattern similar to MC-induction of microsomal enzymes. The effects of MC on serum levels were prevented by previous inj. of D,L-ethionine (200 mg/kg/day, in saline, i.p.). It is concluded that the increased production of Hx is important for induction of microsomal, heme-containing enzymes.

70-1904 BENZOPYRENE HYDROXYLASE ACTIVITY AND ITS INDUCTION BY METHYLCHOLANTHRENE IN MORRIS HEPATOMAS, IN HOST LIVERS, IN ADULT LIVERS, AND IN RAT LIVER DURING DEVELOPMENT. (E.) Watanabe, M. (Tohoku U. Res. Inst. Tuberc. Leprosy Cancer, Sendai, Japan), V. R. Potter and H. P. Morris. *Cancer Res.* 30(2):263-273, 1970.

Benzpyrene hydroxylase (BPH) activity was very low (about 30×10^{-9} M/g liver/hour) in fetal Badger rat livers, markedly increasing after birth. Enzyme activity after induction with 3-methylcholanthrene (MC; 2 mg/100 g body wt.) was significantly increased at all developmental stages and directly related to age, with no difference between male and female animals up to 21 days. The natural and induced levels of BPH in various Morris hepatomas were consistently lower compared to host liver; the different hepatoma lines (9618A, 9633, 7800, 7794A and 8999) showed a significantly different response to MC. Dietary regimen and protein levels had little or no effect on natural and induced levels of BPH in Charles River rats, but host liver in Buffalo rats bearing Morris hepatoma 9618A showed a marked response to different dietary regimens. The enzyme activity in the host liver of rats bearing hepatoma 8999 showed an inverse relationship to the size of the pooled hepatoma mass. Actinomycin D (50 μg /100 g body wt.), puromycin (5 mg/100 g) and cycloheximide (2 mg/100 g) inhibited enzyme induction both in host livers and in hepatomas.

70-1905 CARCINOGENIC ACTIVITY OF 1,2-DIMETHYL-HYDRAZINE IN GOLDEN HAMSTERS. (Ger.) Osswald, H. (German Cancer Res. Ctr., Heidelberg) and F. W. Krüger. Arzneimittelforschung 19(11): 1891-1892, 1969.

The acute i.m. LD₅₀ of 1,2-dimethylhydrazine in golden hamsters was 95 mg/kg. Among animals receiving 4.3 mg/kg/wk i.m. (total 146.2 mg/kg), 10/40 died of liver necrosis and hemorrhage prior to the end of the treatment period; 3/40 died of enteritis and 2/40 died of pneumonia during the same period. Of the animals surviving treatment, 11/25 died of liver damage in the absence of any tumors; 9/25 developed fatal adenocarcinomas of the g.i. tract; 5/15 developed fatal carcinomas of the liver (accompanied by ascites in 2/5). The mean latency period for tumor induction was about 261 days. No tumors or liver damage developed among 12/12 controls.

70-1906 COMPARATIVE CARCINOGENICITY IN THE RAT OF 2-HYDRAZINOTHIAZOLES WITH NITROFURYL, NITROPHENYL, OR AMINOPHENYL SUBSTITUENTS IN THE 4-POSITION. (E.) Cohen, S. M. (U. Wisconsin Med. Sch., Madison), E. Ertürk, J. M. Price and G. T. Bryan. Cancer Res. 30(4):897-901, 1970.

Female Sprague-Dawley rats were fed 2-hydrazino-4-(5-nitro-2-furyl)thiazole (HNT; cumulative dose, 4.2 g/rat), 2-(2,2-dimethylhydrazino)-4-(5-nitro-2-furyl)thiazole (DMNT, 0.8 g/rat), 2-hydrazino-4-(4-nitrophenyl)thiazole (NPT; 7.3 g/rat) or 2-hydrazino-4-(4-aminophenyl)thiazole (APT; 2.4 g/rat), all of which proved to be potent carcinogens. Each induced chiefly mammary gland carcinomas (32/35, 30/31, 27/34 and 34/35, resp.), as well as a lower frequency of tumors of other organs. The number of salivary gland adenocarcinomas induced by HNT, DMNT, NPT and APT was 2, 3, 15 and 3, resp.. The carcinogenic relationship of these 4 agents to formic acid 2-[4-(5-nitro-2-furyl)-2-thiazolyl]hydrazide is discussed.

70-1907 CARCINOGENICITY OF FORMIC ACID 2-[4-(5-NITRO-2-FURYL)-2-THIAZOLYL]-HYDRAZIDE IN SWISS MICE. (E.) Cohen, S. M. (U. Wisconsin Med. Sch., Madison), E. Ertürk and G. T. Bryan. Cancer Res. 30(4):906-912, 1970.

Female 5-week-old Swiss mice were fed formic acid 2-[4-(5-nitro-2-furyl)-2-thiazolyl]hydrazide (FNT; 5.4-6.7 mg/day x 29 weeks, with a cumulative dose of 1.2 g/mouse) and the number of tumors induced was assessed. FNT was strongly carcinogenic and leukemogenic in 21/22 and 19/22 mice, resp. Solid tumors included squamous cell and adenocarcinoma of the stomach (21/22), mammary adenocarcinomas (7/22), alveolar lung carcinomas (9/22) and single tumors of the uterus and skin. In control mice, lung tumors developed in 1/44 and generalized leukemia in 15/44. The molecular

basis of the carcinogenicity of FNT in these mice is unknown.

70-1908 URINARY BLADDER CARCINOGENICITY OF N-[4-(5-NITRO-2-FURYL)-2-THIAZOLYL]-FORMAMIDE IN FEMALE SWISS MICE. (E.) Ertürk, E. (U. Wisconsin Med. Sch., Madison), S. M. Cohen and G. T. Bryan. Cancer Res. 30(5):1309-1311, 1970.

Female 5-week-old Swiss mice were fed N-[4-(5-nitro-2-furyl)-2-thiazolyl] formamide (FANFT; 0.094% by wt. of diet x 46 weeks). Of the mice surviving more than 28 weeks, 31/33 (94%) developed urinary bladder tumors, 23/33 (70%) had generalized leukemia and 6/33 and 1/33 developed tumors of the lung and uterus, resp. Of the controls, 15/44 (35%) had generalized leukemia and 1/44 developed a lung tumor. All of the 11 offspring of FANFT-fed mice developed urinary bladder carcinoma when fed the compound; 1/8 control offspring of FANFT-fed mice had bladder hyperplasia. Presence of forestomach and liver lesions in offspring of FANFT-fed mice indicates a possible active carcinogenic metabolite in the mothers' milk.

70-1909 MALIGNANT LYMPHOMA ASSOCIATED WITH HYDANTOIN DRUGS. (E.) Anthony, J. J. (Cincinnati Gen. Hosp., Ohio). Arch. Neurol. (Chicago) 22(5):450-454, 1970.

A review of over 100 cases of lymphadenopathy as a result of hydantoin therapy revealed about a third with eosinophilia from 7-20%. The onset of symptoms occurred after an av. of 3 mo., but can vary from hours to many yr. No correlation between age and lymphadenopathy exists. Of necropsies performed at Cincinnati General Hospital from 1958-1968, inclusive, 4/85 (4.4%) lymphoma pts. had epilepsy and a long-term history of diphenylhydantoin sodium therapy (10 yr. or more), in comparison to an expected epilepsy frequency for the general population of 1/200 persons. This is about a 10-fold difference, which is considered significant, although it does not prove that lymphoma is caused by hydantoins.

70-1910 THE RELATIONSHIP BETWEEN SOME ANTI-CONVULSANTS AND TUMORS OF THE BLOOD FORMING ORGANS. (E.) Bercel, N. A. (U. Southern California Sch. Med., Los Angeles) and H. H. Henstell. Bull. Los Angeles Neurol. Soc. 35(1): 21-24, 1970.

A history of admin. of anticonvulsants (paramethadione, phensuccimide, trimethadione, diphenylhydantoin sodium, etc.) to 2 pts. with epilepsy is discussed in relation to the development of abnormal WBC counts, depression of polymorphonuclear leukocytes and neutropenia and the possible malignant transformation to

phoma in 1 case. Examples are also given of
g-induced lymphadenopathy and pseudolymphoma
olving mephenytoin and phenobarbital admin.
is suggested that, in some genetically-
ceptible pts., admin. of certain anticonvul-
ts is carcinogenic for the blood-forming
ans.

1911 MULTIPLE AETIOLOGICAL FACTORS IN A
CASE OF ACUTE LEUKAEMIA. (E.) Hamer,
W. (Christchurch Hosp., New Zealand) and F. W.
z. New Zeal. Med. J. 71(454):141-142, 1970.

te myelomonocytic leukemia, following marrow
oplasia, was diagnosed in a 47-yr.-old man
had been treated with phenylbutazone (PB;
al dose unknown) for intermittent back pain
ce age 18 yr. A study of the family history
ealed that his father had died of acute
nucloytic leukemia at age 68 yr. It is
gested that the PB altered bone marrow and
uced a genetically-predisposed mutation leading
development of leukemia.

1912 LACK OF EFFECT OF DIPHENYLHYDANTOIN
INGESTION ON VESICAL TRANSITIONAL
THELIUM IN THE RAT. (E.) McDonald, D. F.
Texas Med. Branch, Galveston). J. Surg. Oncol.
):77-79, 1969.

enling Long-Evans rats were divided into 2
ups (Group 1 had no vesical foreign body;
up 2 received a surgically implanted 3 mm
vesical glass bead) and then admin. diphenyl-
antoin (DH; 0.02% x 1 mo., then 0.04% x 11 mo.,
he diet). Results showed 1/37 DH-treated
s of Group 1 and 11/27 DH-treated rats of
up 2 to have developed vesical calculi. No
elastastic lesions were seen in any of the 27
s of Group 2. The transitional epithelium
a normal in the 37 rats of Group 1 and in the
ats of group 2 that did not develop calculi.
ts suggested that DH is not tumorigenic to
ositional epithelium and that bladder tumors
h develop in pts. who are chronically treated
DH are probably coincidental.

1913 AFLATOXIN-INDUCED HEPATIC INJURY IN
THE AFRICAN MONKEY. (E.) Alpert, E.
achusetts Gen. Hosp., Boston), A.
ek-Hanssen and B. Rajagopalan. Arch. Environ.
e th (Chicago) 20(6):723-728, 1970.

g male *Cereopithecus aethiops* African monkeys
e fed aflatoxin (0.01-1 mg/day in corn oil by
aric intubation). Liver histological changes
e identical for 3/5 monkeys. Changes included
ection of eosinophilia, disappearance of
u coli, fatty changes, pigmentation of areas
f liver damage, degeneration and necrosis.
ough the number of animals is small, the
tical results in 3 monkeys support a con-
ion that aflatoxin induced changes in the
ir.

70-1914 AFLATOXIN-INDUCED FATAL HEPATITIS? A
CASE REPORT FROM UGANDA. (E.)

Serck-Hanssen, A. (Ullevål Hosp., Oslo). Arch.
Environ. Health (Chicago) 20(6):729-731, 1970.

A 15-yr.-old African boy with acute hepatic
disease was diagnosed as having died of hepatitis
due to ingestion of aflatoxin in the diet when
changes in the liver tissue resembled those for
experimental, aflatoxin-treated African monkeys.
It is suggested that autopsy and biopsy studies
look for evidence of aflatoxin-induced liver
injury in cases of hepatic disease.

70-1915 STUDY OF LIVER INJURY IN MICE FED WITH
SPOILED GROUNDNUTS. (E.) Syamasundara
Rao, P. (Guntur Med. Coll., India). J. Indian
Med. Ass. 54(1):6-11, 1970.

Male and female, 128-239-day-old, Swiss albino
mice were fed a basic diet mixed with spoiled
peanuts (20-50%), contaminated by various strains
of fungi and ranging from slightly to highly
spoiled condition. Hepatic cell necrosis, high
mitotic activity and regenerative hyperplasia
resulted for all animals fed the spoiled peanuts.
Fatty changes occurred in all but the mice fed
a 20% moderately-spoiled peanut diet and the
controls. It is suggested that natural aflatoxins
produced by fungi are causative factors in
hepatic disease.

70-1916 THE EFFECT OF AFLATOXIN B₁ ON AMEBAE.
(Ger.) Bauer, L. (U. Erlangen-Nurnberg
Path. Inst., Erlangen, Germany) and L. Leistner.
Arch. Hyg. Bakt. 153(5):397-402, 1969.

When *Limax*-type amebae, feeding on *E. coli* in an
aqueous medium in agar-coated Petri dishes, were
exposed to aflatoxin B₁ (2.0, 20.0 or 50.0
µg/ml agar), buds formed on day 3 or later
fter the addition of the crystalline compound
to the agar, degenerated shortly after they
appeared, followed by lysis of the parent cell.
A similar effect was not seen at a conc. level
of 0.2 µg/ml agar (0.2 ppm). At the higher
conc. levels, parent cells transferred to a
toxin-free medium immediately after degeneration
of the buds failed to undergo lysis and developed
into normally-growing cultures. No effect was
exerted by the toxin on amebae in a vegetative
state, although the growth rate of such cultures
was slightly reduced during the first 2 days of
exposure to conc. of 2.0 µg/ml agar or more.
Replication of *E. coli* in the toxic medium was
unaffected at any conc. level.

70-1917 THIN LAYER CHROMATOGRAPHIC SEPARATION
OF AFLATOXINS ON SILICA GEL PLATES.
(Ger.) Reiss, J. (Grahamhaus Studt KG Microbiol.
Lab., Bad Kreuznach, Germany). J. Chromatogr.
49(2):301-303, 1970.

A comparative study using 5 different ready-made silica gel plates and a number of different solvents revealed that the best separation of aflatoxins was obtained using the Polygram Sil N-HR plate and a 3:97 methanol-chloroform solvent mixture. An R_f value of 0.49 for aflatoxin B₁ and of 0.40 for aflatoxin G₁ was obtained.

70-1918 AFLATOXIN DETERMINATIONS IN ANIMAL

FEEDS: RESULTS AND PROBLEMS. (Ger.)

Jost, R. (U. Bern Vet. Bact. Inst., Switzerland) and J. Nicolet. Path. Microbiol. (Basel) 33(5): 296-307, 1969.

Alternative methods are described for detecting the presence of aflatoxins in industrial feeds and assaying the quantities present. In tests relying on visual discrimination of fluorescent spots on thin-layer chromatography plates, even experienced operators gave 20%-30% misreadings, although 70% of a group of inexperienced operators remained within about a 33% margin of error. In tests involving recovery by extraction and purification (the Nesheim method), mean recoveries were between 50%-60%, with a range of 40%-100%. The chief source of error was the fact that about 25% of the solvent was retained in the sediment, following centrifugation. Analyses of both complex feeds and individual components were impeded by the presence of fluorescent substances in the extracts which interfered with the aflatoxins during thin-layer chromatography. Such interference was compensated partially by the addition of known quantities of pure aflatoxins to the extracts. Both chemical spot tests and biologic "confirmation" tests employing *B. megaterium* or other bacilli lacked specificity.

70-1919 SPECTRAL STUDIES ON THE DEOXYRIBONUCLEIC ACID-AFLATOXIN SYSTEM. BINDING INTER-

ACTIONS. (E.) Neely, W. C. (Auburn U., Ala.), J. A. Lansden and J. R. McDuffie. Biochemistry (Wash.) 9(8):1862-1866, 1970.

Studies of fluorescence polarization in mixtures of DNA and aflatoxin B₁ showed an increased polarization with viscosity. Fluorescence intensities of various aflatoxin-DNA mixtures indicated weak and reversible binding. Low-temperature emission studies were performed to identify the mechanism by which DNA quenches bound aflatoxin luminescence. It is concluded that bound aflatoxin molecules do not fluoresce and that any fluorescence observed was from those molecules in soln. Also, some photo-degradation of aflatoxin during its binding activity is suggested.

70-1920 TIME COURSE AND DOSE-RESPONSE

CHARACTERISTICS OF AFLATOXIN B₁.

EFFECTS ON RAT LIVER RNA POLYMERASE AND ULTRA-STRUCTURE. (E.) Pong, R. S. (Massachusetts Inst. Technol., Cambridge) and G. N. Wogan. Cancer Res. 30(2):294-304, 1970.

DNA-dependent RNA polymerase activity (Mg^{+2} -activated) in the liver of male Fischer rats (100 g) inj. with aflatoxin B₁ (1 mg/kg, i.p.) was suppressed 60% within 15 min., reaching a max. depression in 12 hours and returning to control levels at 36 hours. RNA polymerase activated by Mn^{+2} -(NH_4)₂SO₄ was similarly inhibited. Nuclear RNA/DNA ratio after 15 min. was 0.169 in the treated rats as compared to 0.237 in controls; the loss of nuclear RNA was max. in 12 hours (0.146) and returned to normal at 36 hours. The amount of inhibition correlated significantly with dose of aflatoxin. Nuclear changes concomitant with inhibition of RNA are described.

70-1921 IN VIVO REACTIONS OF β -PROPIOLACTONE.

(E.) Boutwell, R. K. (U. Wisconsin

McArdle Lab., Madison), N. H. Colburn and C. C. Muckerman. Ann. NY Acad. Sci. 163(2):751-763, 1969.

In the study of the molecular mechanism of mouse skin carcinogenesis by β -propiolactone (PL) *in vivo*, binding of PL to DNA, RNA and protein increased linearly for PL doses up to 480 μ M. On a per-gram-basis, binding to protein was double the binding to DNA or RNA. Max. tumor incidence also occurred at the 480 μ M dose level. Results show 7-(2-carboxyethyl)guanine to be the major binding product of PL with both DNA and RNA. Carboxyethyl-cysteine was found in the acid hydrolysate of protein isolated from the skin of PL-treated mice. Experiments using STS mice treated with PL, 3-iodopropanoic acid, 3-chloropropanoic acid (120 μ M, 2 admin./week x 3 weeks) or iodoacetic acid (10 μ M, same regimen) followed by repeated applications of croton oil showed PL to be clearly more effective than iodopropanoic acid as an initiator (7.1 and 0.7 papillomas/mouse at 22 weeks, resp.); iodoacetic acid and chloropropanoic acids being ineffective. There was a strong correlation of DNA binding with tumor-initiating property, thus supporting DNA as the significant cellular receptor of carcinogenic alkylating agents. Template activity of alkylated DNA in an RNA polymerase system is defective, although no difference was detected in the level of transcription error of normal or alkylated DNA.

70-1922 A PRELIMINARY EXPERIMENTAL STUDY OF POSSIBLE CARCINOGENIC ACTIONS OF

"BUTAZOLADIN" (3,5-DIOXO-1,2-DIPHENYL-4-n-BUTYLPIRAZOLIDINE) AND "UROTROPIN" (HEXAMETHYLENETETRAMINE) IN RATS. (Por.) De Azavedo e Silva E. (Fed. U. Pernambuco Fac. Med., Brazil). An. Fac. Med. Pernambuco 26(7):25-32, 1966/67.

A group of 24, 60-day-old male and female Wistar rats was inj. with phenylbutazone (60 mg/kg/day x 30 days, i.p.) and others were inj. with methenamine (200 mg/kg/day, same as above); they were maintained for 14 mo. and examined by autopsy for neoplasms. The number of animals

too small to state that there was no significant increase in development of neoplasms due to these compounds.

1923 CARCINOGENIC EFFECTS OF 3,3'-BENZIDINEDICARBOXYLIC ACID. (Rus.) Pliss, G. B. N. Petrov Sci. Res. Inst. Oncol., Leningrad, (R). Vop. Onkol. 15(5):60-64, 1969.

Male and female Rappolovo rats (total 55) were admin. 3,3'-benzidinedicarboxylic acid (BDC; 20 mg/week x 22 mo.; in sunflower oil, s.c.) and 13 surviving rats developed tumors in 18-21 mo. (1 leukemia, 1 adenocarcinoma of the cecum, 2 mammary tumors). Of 60 mice admin. BDC (5 mg/week x 20.5 mo., s.c.), 6/27 survivors developed tumors (4 liver tumors, 1 sarcoma of s.c. tissue, 1 leukemia); after 14-22.5 mo. of 60 mice treated with BDC (2 mg, 6 admin./week x 15 mo., p.o.), 17 survivors developed tumors (1 leukemia, 5 hemangiomas, 2 hemangiomas combined with hepatoma, 1 malignant adenoma of the stomach) in 10.5-20 mo. Admin. of the sodium salt of BDC (BDC-Na; 5 mg/week x 22 mo., s.c.) to 57 rats induced tumors in 7/17 survivors (3 Zymbal gland tumors, 2 fibroadenomas of the mammary glands, 1 squamous cell cancer, 1 sarcoma of the thymus) in 18-26.5 mo. Of 55 mice treated with BDC-Na (5 mg/week x 20.5 mo., s.c.), 6/32 survivors developed tumors (1 leukemia, 3 lung adenomas) in 10-21 mo. Liver hemangiomas were 6-7-fold more frequent in BDC-Na-treated animals, while leukemia and lung adenomas developed at the same frequency in treated and control animals.

1924 BIOCHEMICAL AND PATHOLOGICAL EFFECTS OF METHYLAZOXYMETHANOL ACETATE, A POTENT CARCINOGEN. (E.) Zedeck, M. S. (Sloan-Kettering Inst. Cancer Res., New York, N. Y.), S. Sternberg, R. W. Poynter and J. McGowan. Cancer Res. 30(3):801-812, 1970.

Protein and nucleic acid syntheses in liver, small intestine and kidney of Sprague-Dawley rats and CD1 mice were studied after admin. of methylazoxymethanol acetate (MAM; 35 or 50 mg/kg in rats, 25 mg/kg in mice; i.v.). In rats, early inhibition of thymidine incorporation into DNA was seen, and the liver was the organ that showed marked inhibition of RNA and protein synthesis. In mice, liver was more sensitive than kidney or small intestine and showed inhibition of RNA and protein synthesis; changes occurred in kidney or small intestine. In rats, 6 hours after MAM admin., there was minimal focal necrosis in liver; the duodenum and colon showed marked karyorrhexis in crypt epithelium. Within 1 week there was intestinal atrophy, but hepatic nuclear changes, including enlarged and irregular nuclei, occurred after 1 mo. Microsegregation in rat hepatic cells occurred within 1 hour after treatment, and there was more inhibition of nuclear RNA synthesis, and acinar change persisted for several mo. Mouse

liver showed necrosis, but duodenal changes were minimal. In both mice and rats, kidneys were normal at all times. Relationships between pathology, carcinogenesis and inhibition of synthesis of various macromolecules are also discussed.

70-1925 REPRESSION OF BENZO(a)PYRENE TUMORIGENESIS IN HAMSTERS BY PRETREATMENT WITH CELLS INFECTED OR TRANSFORMED BY TYPE 12 ADENOVIRUS. (E.) Pinkerton, H. (St. Louis U. Sch. Med., Mo.) and P. I. S. Liu. Fed. Proc. 28(2):750, 1969.

70-1926 LASER EFFECT ON DMBA-INDUCED DYSKERATOSES OF THE HAMSTER CHEEK POUCH. (E.) Gordon, T. E., Jr. (550 N. Bumby Ave., Orlando, Fla.), C. A. Wladron and L. S. Gordon. Cancer 25(4):851-857, 1970.

70-1927 OBSERVATIONS OF THE EFFECT OF DIETHYLNITROSAMINE ON GLUCURONIDE FORMATION. (E.) Mowat, A. P. (U. Aberdeen, Scotland) and I. M. Arias. Biochim. Biophys. Acta 212(1):175-178, 1970.

70-1928 GLUCOSE-6-PHOSPHATASE AND ALDOLASE IN RAT LIVER TUMORS INDUCED BY DIETHYLNITROSAMINE. (Ger.) Hadjiolov, D. (ul. Plovdivsko pole 6, Sofia-Darvenitza, Bulgaria) and A. Dikow. Z. Krebsforsch. 74(1):46-54, 1970.

70-1929 CODING PROPERTIES AND CIRCULAR DICHROISM (CD) SPECTRA OF OLIGONUCLEOTIDES MODIFIED WITH N-2-ACETYLAMINOFLUORENE (AAF). (E.) Grunberger, D. (Columbia U., New York, N. Y.), J. H. Nelson, C. R. Cantor and I. B. Weinstein. Fed. Proc. 29(2):883, 1970.

70-1930 STIMULATION OF DNA SYNTHESIS OF RAT SALIVARY GLAND CELLS IN MONOLAYER CULTURES BY ISOPROTERENOL. (E.) Kreider, J. W. (Pennsylvania State U. Coll. Med., Hershey). Cancer Res. 30(4):980-983, 1970.

70-1931 INHIBITORY EFFECT OF URINARY ASCORBATE ON TUMOR FORMATION IN MICE BLADDERS IMPLANTED WITH PELLETS CONTAINING 3-HYDROXY-ANTHRANILIC ACID. (E.) Pipkin, G. E. (Tulane U. Sch. Med., New Orleans, La.), J. U. Schlegel, R. Nishimura and G. N. Shultz. Fed. Proc. 28(2):889, 1969.

70-1932 THE METABOLISM OF THE 8-METHYL ETHER OF XANTHURENIC ACID (XAE) IN RABBITS. (E.) Lower, G. M., Jr. (U. Wisconsin Med. Sch., Madison) and G. T. Bryan. Fed. Proc. 28(2):873, 1969.

70-1933 STUDIES ON INHIBITION OF HORMONE INDUCTION OF TRYPTOPHAN OXYGENASE BY THIOACETAMIDE. (E.) Kizer, D. E. (Samuel Roberts Noble Found., Inc., Ardmore, Okla.), B. Cox and B. C. Shirley. Fed. Proc. 28(2):867, 1969.

70-1934 TRACE METAL ANALYSIS OF CANCEROUS AND NONCANCEROUS HUMAN TISSUES. (E.) Mulay, I. L. (Pennsylvania State U., University Park), R. Roy, B. E. Knox and N. H. Suhr. Fed. Proc. 28(2):692, 1969.

70-1935 EFFECT OF SINGLE AND FRACTIONATED DOSES OF METHYLNITROSOUREA ON THE MORTALITY AND INCIDENCE OF MALIGNANT LYMPHOMAS IN ADULT SWISS MICE. (E.) Joshi, V. V. (U. Western Ontario Cancer Res. Lab., London, Canada) and J. V. Frei. Fed. Proc. 29(2):490, 1970.

70-1936 CARCINOGENICITY OF 6 β -HYDROXY-4-CHOLESTEN-3-ONE IN FEMALE MARSH MICE.

(E.) Bischoff, F. (Santa Barbara Cottage Hosp. Res. Inst., Calif.) and G. Bryson. Fed. Proc. 29(2):860, 1970.

70-1937 BIOLOGICAL ACTIVITY OF SYNTHETIC, RACEMIC AFLATOXIN B₁. (E.) Pong, R. S. (Massachusetts Inst. Technol., Cambridge) and G. N. Wogan. Fed. Proc. 29(2):568, 1970.

70-1938 AFLATOXIN METABOLISM IN THE RAT AND MOUSE LIVER. (E.) Campbell, T. C. (Virginia Polytech. Inst., Blacksburg) and R. S. Portman. Fed. Proc. 29(2):567, 1970.

70-1939 RAT LIVER PLASMA MEMBRANES IN CHEMICAL CARCINOGENESIS. (E.) Chandrasekhara, N. (U. Illinois Burnside Res. Lab., Urbana) and K. A. Narayan. Fed. Proc. 29(2):865, 1970.

70-1940 RIBOFLAVIN AND AZO DYE INDUCED HEPATOMAS IN THE RAT. (E.) Lambooy, J. P. (U. Maryland, Baltimore). Fed. Proc. 29(2):296, 1970.

See also abstract nos: 1713, 1714, 1715, 1716, 1717, 1719, 1720, 1724, 1725, 1727, 1747, 1748, 1960, 1971, 1977, 1992, 1995, 2000, 2002, 2010, 2014, 2024, 2033, 2066, 2067, 2070, 2071, 2072, 2081, 2082, 2083, 2084, 2087, 2109, 2113

1941 REPLICATION OF ROUS SARCOMA VIRUS IN SYNCHRONIZED CELLS. (E.) Hobom-Schnegg, (Stanford U., Palo Alto, Calif.), H. L. Ineson and W. S. Robinson. J. Gen. Virol. 1:85-93, 1970.

chick embryo cells, synchronized in tissue culture, were infected with the Bryan high-titer strain of Rous sarcoma virus (RSV) when the cells were in the pre-DNA synthesis period (G-1) during the period of DNA synthesis (S). The number of foci were found in each culture after 6 days, but virus production was delayed several hours in cells infected at G-1; this was due to a change in rate of virus adsorption and penetration. Similar experiments using the Rous strain of Newcastle disease virus showed virus to be independent of the cell division cycle. The ability of the cells to eloop foci and to produce virus decreased with time when cells were infected with RSV at various time intervals after peak DNA synthesis. Cells cultured more than 15 hours lost susceptibility to RSV.

1942 A STUDY OF SURFACE IONOGENIC GROUPS OF CHICK EMBRYO CELLS TRANSFORMED BY ROUS SARCOMA VIRUS. (E.) Patinkin, D. (Hebrew U. Jerusalem Med. Sch., Jerusalem), A. Zaritsky and J. Doljanski. Cancer Res. 30(2):498-503, 1970.

A significant difference in electrophoretic mobility was found in cells from 9-10-day-old chick embryo cells transformed by Rous sarcoma virus (Bryan high-titer strain) and corresponding normal cells derived from the same embryos. The mobility relationships for transformed and normal cells were identical (positive between pH 2.0-3.6 and negative between pH 3.9-8.0), as was the reduction in electrophoretic mobility with the addition of calcium ions (from 5×10^{-6} to 4.8×10^{-3} M). Treatment with neuraminidase produced a reduction in the mobility of transformed cells equal to or less than that of normal cells. No generalization could be made as to the correlation between malignancy, increased surface charge density and increased surface sialic acid.

1943 OBSERVATIONS ON THE ENVELOPE PROPERTIES OF RSV(0). (E.) Ishizaki, R. (Nat. Inst. Anim. Health, Kodaira-shi, Tokyo) and T. Mizu. Virology 40(2):415-417, 1970.

Chick embryo fibroblasts of the C/A and C/O genotype, derived from line 15-1 chickens, were resistant to infection with the Bryan strain of Rous sarcoma virus RSV(0) while cell cultures of Japanese quail were susceptible. The C/O cells, however, became highly susceptible after pre-infection with subgroup A avian leukosis viruses; C/O cells derived from other chicken lines

showed no loss of resistance. No neutralization of RSV(0) was observed using chicken antisera against virus subgroup A, B and D and pigeon sera containing group-specific antibody. Quail sera against RSV(0) neutralized the virus to a level of about 10% survivors.

70-1944 SYNTHESIS OF THE RNA OF RNA-CONTAINING TUMOR VIRUSES. I. THE INTERVAL BETWEEN SYNTHESIS AND ENVELOPMENT. (E.) Bader, J. P. (NCI, Bethesda, Md.). Virology 40(3):494-504, 1970.

RNA was radioactively labeled in chick embryo cells infected with Rous sarcoma virus-Rous associated virus, and in mouse splenic cells producing mouse Rauscher leukemia virus; the virus was separated by sucrose gradient centrifugation, and viral RNA was analyzed by electrophoresis on polyacrylamide gels. Radioactive viral RNA was found as early as 2 hours after introduction of the label, and reaching a maximum within 5 hours; the minimal interval between labeling of viral RNA and its appearance in virus was estimated to be about 70-75 hours. Antagonists of RNA (actinomycin D) and protein synthesis (puromycin and cycloheximide) prevented production of infectious virus only when given within 15 min. after the label. This indicates an inhibition of synthesis of viral components rather than inhibition of virion assembly.

70-1945 EFFECT OF AGAR, CALF EMBRYO EXTRACT, AND POLYANIONS ON PRODUCTION OF FOCI OF TRANSFORMED CELLS BY ROUS SARCOMA VIRUS. (E.) Vigier, P. (Inst. Radium, Orsay, France). Virology 40(2):179-192, 1970.

Medium gelled by unwashed agar (UWA) or supplemented with UWA extract or calf embryo extract (CEE) stimulated an increased number of foci produced by the Bryan strain of Rous sarcoma virus (Rous associated virus 1) in chick embryo cells compared to standard media gelled by washed agar or agarose. Addition of increasing conc. of UWA or CEE to the standard media caused a linear increase in the number of foci up to the maximum number obtainable; this increase was observed up to 6 days after infection. The production of virus was little affected by CEE or UWA initially, but a 2-4-fold increase in titer and number of infective centers was seen after 6 days. CEE and UWA also reversed the suppression of foci by fetal calf serum. It is suggested that they favor cell transformation. The active factor in CEE and UWA was hydro-soluble, thermostable and nondialyzable; removal of the active factor by diethylaminoethyl-dextran and enhancement of focus-formation by dextran sulfate (not hyaluronic acid) indicated it was an acid polysaccharide. Limited focus-promoting effect on the Schmidt-Ruppin strain of Rous sarcoma virus was seen.

70-1946 THE HOST RANGE OF BRYAN STRAIN ROUS SARCOMA VIRUS SYNTHESIZED IN THE ABSENCE OF HELPER VIRUS. (E.) Weiss, R. A. (Univ. Coll. London). J. Gen. Virol. 5(4): 511-528, 1969.

Rous sarcoma virus (0) (RSV(0)) was tested in various leukosis virus-negative fowl cells and found to be infectious for Japanese quail, European pheasants and partially in Brown Leghorns, White Leghorns and Reaseheath 1 x C hybrids; the host range was distinct from other subgroups of avian tumor viruses. The differences in susceptibility in Brown Leghorns were not caused by variable assay conditions, but were assumed to be genetically controlled. No sex linkage was found. The RSV(0) synthesized by the Brown Leghorn lines produced infectious virus (designated RSV β (0)) with the same host range as the parental virus, but non-infectious virus (RSV α (0)), detectable by electron microscopy, was synthesized by all Reaseheath C and quail lines tested. No natural host for RSV α (0) has been found, with 1 possible exception. The host cell synthesizing the RSV(0) determined the infectivity, possibly by modulating between α and β ; this was seen when RSV β (0) cloned in quail or Reaseheath C lines lost its infectivity and became RSV α (0), and conversely, RSV β (0) was produced from an RSV α (0) infection in Brown Leghorns.

70-1947 INTERFERENCE AND NEUTRALIZATION STUDIES WITH BRYAN STRAIN ROUS SARCOMA VIRUS SYNTHESIZED IN THE ABSENCE OF HELPER VIRUS. (E.) Weiss, R. A. (Univ. Coll. London). J. Gen. Virol. 5(4):529-539, 1969.

Secondary cultures of Brown Leghorn fibroblasts were infected with subgroups A, B and C leukosis viruses (Rous associated virus 1 (RAV1), RAV2 and RAV50, resp.) and tested for interference with Rous sarcoma virus (RSV) β (0). RAV2 strongly inhibited infection with RSV β (0) while the others did not, but the host range for subgroup B viruses differed in that they were not infectious for quail cells. Immunization studies showed RSV β (0) was inhibited only by its own antisera and anti-RSV β (0) partially inhibited RSV(RAV)2; antisera against the Schmidt-Ruppin strain of RSV (Harris strain, provisionally called subgroup D) was active against RSV β (0). Inoc. of RSV β (0) into most chickens and quail did not stimulate synthesis of antiviral antibodies. Transplantation immunity was also weak. No helper virus in RSV β (0) was demonstrated.

70-1948 EVIDENCE FOR THE DEFECTIVENESS OF THE HARRIS STRAIN OF ROUS SARCOMA VIRUS. (E.) Reamer, R. H. (US Dept. Agric. Res. Serv., Washington, D. C.) and W. Okazaki. J. Nat. Cancer Inst. 44(4):763-767, 1970.

Viral interference and neutralization tests demonstrated Rous-associated virus (RAV-6), a

noncytopathic avian leukosis virus isolated from the Harris strain of Rous sarcoma virus (HA-RSV), to be antigenically identical to HA-RSV. Four transformed cell clones, the supernatant of which produced no neoplastic changes on chick embryo fibroblasts (CEF) susceptible to all known avian leukosis-sarcoma viruses (C/0), were derived from HA-RSV-infected C/0 CEF by use of feeder layers of duck embryo fibroblasts. Activation by all 8 strains of avian leukosis viruses tested occurred in 1/4 of these clones; the activation potential of this clone approached that of leukosis negative Rous cells derived from the Bryan high-titer (BH) strain of RSV. Low or no activating potential was seen in 3/4 clones. It is suggested that the HA-RSV is defective in a way similar to BH-RSV.

70-1949 USE OF INFECTIOUS AND ONCOGENIC VIRUSES AS HELPERS FOR DEFECTIVE ROUS VIRUS. (Rus.) Kuznetsov, O. K. (N. M. Petrov Sci. Res. Inst. Oncol., Leningrad, USSR). Vop. Virus 14(4):393-397, 1969.

In chick embryo cultures infected with Rous sarcoma virus (RSV, Bryan strain), 48 foci of transformed cells were located which were then cultivated in the presence of normal chick fibroblasts. Foci of transformation were found in 43 cultures and classified as non-producing (14.6%), low-producing (29.1%) or high-producing (45.8%). In 5 cultures, transformation foci were absent, though culture fluid of 3/5 was infectious for normal cells. In a study of the effects of latent avian leukosis virus (ALV) and Rous associated virus (RAV) on the defective RSV, admin. of ALV or RAV to the non-producing cultures caused appearance of active RSV, whereas admin. of infectious parotitis virus (IPV) and Sendai virus (SV) had no such effect. RSV content increased 10-1000-fold when ALV and RAV were admin. to low-producing cultures. In high-producing cultures, ALV and RAV did not stimulate RSV, and IPV and SV inhibited RSV reproduction 10-100-fold.

70-1950 GENETIC RESISTANCE OF FOWL TO MH2 RETICULOENDOTHELIOMA VIRUS. (E.) Payne, L. N. (Houghton Poultry Res. Station., Huntingdon, England) and P. M. Biggs. J. Gen. Virol. 7(3):177-185, 1970.

The host range of the MH2 (Mill Hill 2) strain of avian tumor virus on embryos of Reaseheath C, 1, R and W Leghorns, Houghton Brown Leghorns and Sykes's Line B Rhode Island Reds was compared to known subgroup A, B and C strains of Rous sarcoma virus (RSV) and placed in subgroup C. This was confirmed by virus interference tests and immunological relationships with subgroup C RSV. Crosses between the Reaseheath R line (resistant to MH2) and the W line (susceptible) indicate that a single autosomal recessive gene controls resistance to MH2.

-1951 CYTOLOGY AND GROWTH CHARACTERISTICS OF HUMAN TUMOUR ASTROCYTES TRANSFORMED BY RSV SARCOMA VIRUS. (E.) MacIntyre, E. H. (U. Colorado Med. Ctr., Denver), R. A. Grimes and E. Vatter. J. Cell Sci. 5(3):583-602, 1969.

a fully transformed cell complex of EH-118MG cells (human tumor astrocyte strain 118 MG transformed by the Engelbreth-Holm strain of Rous sarcoma virus) appeared as a surface monolayer of stellate cells interspersed by pleomorphic giant cells, and a basal monolayer of numerous colonies of round cells with similar free cells in the medium. The round cells and stellate cells multiplied at comparable rates, each was able to synthesize DNA and undergo mitosis, and cell cultures formed by either gave similar results. Indirect fluorescence microscopy showed group-specific antigen in the cytoplasm of all transformed cells, but investigation by electron microscopy and direct fluorescence for virus particles was negative. Inj. of $1-2 \times 10^6$ EH-118MG cells s.c. in Hyline chickens produced Rous sarcomas in 7/25, while no tumors were produced by similar inj. of 118MG cells. The morphological characteristics of the 118MG cells and the transformed cells are also compared.

-1952 INVESTIGATIONS ON VIRUS PRODUCTION IN RSV MAMMALIAN TUMOURS. (E.) Gelderblom, H. (Max Planck Inst. Virus Res., Tubingen, Germany), H. Bauer and H. Frank. J. Virol. 7(1):33-45, 1970.

Tumor lines were induced in inbred STU mice by i.p. inoc. with Schmidt-Ruppin (SR) strain Rous sarcoma virus (RSV)-transformed chick cells and were subsequently passaged in adult STU mice. In these tumors demonstrated group-specific complement-fixing antigen, tumor specific transplantation (TST) antigen, and back-transfer to chickens, but no viral particles were observed in more than 9500 cell sections under the electron microscope. The RVP₃ tumor cell line induced in C57BL/6 mice by Prague strain of RSV) only showed TST antigen and the RSH tumor line induced in hamsters by a SR-RSV) demonstrated complement-fixing antigen and back transfer. Mature Type C particles, similar to those seen in mouse leukemia virus, were seen in sections of RVP₃ tissue and smaller particles were seen in sections of RSH tumor tissue.

-1953 LEUKEMOID CHANGES INDUCED IN GERMFREE AND CONVENTIONAL RATS BY ROUS SARCOMA VIRUS. (E.) Pollard, M. (U. Notre Dame Lobund Lab., Ind.). J. Reticuloendothel. Soc. 7(2):44-463, 1970.

born germfree Wistar and Sprague-Dawley rats inoc. with the Schmidt-Ruppin strain of Rous sarcoma virus (SR-RSV; 0.1 ml, s.c.) developed multiple cysts and transplantable metastasizing fibrosarcomas. As the tumors enlarged the WBC

counts were elevated up to $300,000/\text{mm}^3$ (with 85% of the WBC being mature neutrophilic polymorphonuclear leukocytes). Spleens were enlarged and myelopoietic foci developed in the livers. High blood cell counts returned to normal after excision of tumor but not after excision of spleen. Transplantation of cells from the enlarged spleens failed to produce leukemoid lesions. Results with conventional rats were similar.

70-1954 ELECTRON MICROSCOPIC STUDIES ON VIRUS PRODUCTION IN ROUS SARCOMAS. (Ger.) Gelderblom, H. (Max Planck Inst. Virus Res., Tubingen, Germany) and H. Bauer. Zbl. Bakt. [Orig.] 212(2-4):400-406, 1970.

Different tests with several mouse Rous sarcoma (RS) tumor lines and a chick tumor line revealed the presence of the group-specific antigen, tumor specific transplantation antigen and virus genome in all mouse tumor lines. In contrast to the chick tumor line, those from the mouse did not contain infectious virus particles. The absence of infectious or defective (not infectious for chick cells) RS virus particles in mouse RS lines was confirmed by electron microscopic examination. The transformed mouse and avian cells and the production of virus particles by the avian sarcoma cells are described. It is suggested that the viral etiology of some tumors induced by RNA viruses can be determined (as for some DNA virus tumors) not by the presence of mature virus particles but by the presence of certain products of the viral-gene functions. It is concluded that virus production is not a prerequisite for the growth of these tumors.

70-1955 EFFECT OF PROLONGED INTERFERON TREATMENT ON MOUSE EMBRYONIC FIBROBLASTS TRANSFORMED BY MURINE SARCOMA VIRUS. (E.) Chany, C. (Nat. Inst. Health Med. Res. Paris) and M. Vignal. J. Gen. Virol. 7(3):203-210, 1970.

Balb/c mouse embryonic fibroblasts, transformed by Moloney sarcoma virus (MSV) and grown in the presence of interferon (IF^+), differed from the original MSV cells in that epithelial cells were more prominent than spindle cells, contact inhibition reappeared, and there were 10-fold more Type C particles, but the Moloney transplantation antigen and the group antigen persisted. When interferon was omitted for 30 passages (IF^0), the cells retained morphological, growth and antigenic characteristics, but a greater number gave rise to colonies in soft agar. The MSV- IF^+ cells were least sensitive to exogenous interferon, and MSV- IF^+ and IF^0 cells, after challenge with Newcastle's disease virus, produced 10-fold more interferon than the original MSV cells, with no refractory state.

70-1956 THE ROLE OF DNA SYNTHESIS IN VIRUS REPLICATION AND THE MORPHOLOGICAL TRANSFORMATION OF NORMAL MOUSE EMBRYO CELLS BY MSV (MOLONEY). (E.) Bather, R. (Nat. Cancer Inst. Canada Saskatchewan Res. Unit, Saskatoon) and A. Leonard. J. Gen. Virol. 7(3):249-256, 1970.

Incubation of 15-day Swiss mouse embryo fibroblasts with cytosine- β -D-arabinofuranoside (ara-C; 10^{-6} - 10^{-3} M) caused an inhibition of DNA synthesis and cell growth, but was reversible with addition of deoxycytidine hydrochloride (dC; 10^{-2} M). Pretreatment for 6 hours with 10^{-3} M ara-C markedly reduced transformation with Moloney sarcoma virus (MSV), but a 10-fold excess of dC restored the transformation to control levels; ara-C was most effective at inhibiting transformation when given within 6 hours after infection. Transformed MSV-producing cells, after X-irradiation (5000 or 100,000 roentgens), could still produce virus after 24 hours with almost the efficiency of untreated cells; 10% were still producing virus after 48 hours. The results indicate that an early DNA synthetic event is required for MSV infection and transformation, and that, once initiated, virus growth no longer depends on DNA synthesis.

70-1957 PATHOLOGIC AND VIROLOGIC STUDIES OF TUMORS INDUCED IN MICE BY TWO STRAINS OF MURINE SARCOMA VIRUS. (E.) Simons, P. J. (Sch. Med., Perth, Australia) and D. J. McCully. J. Nat. Cancer Inst. 44(6):1289-1303, 1970.

Newborn Prince Henry mice were inoc. with Moloney sarcoma virus (MSV; 0.03 ml, i.m., s.c. or i.p.) or Harvey sarcoma virus (HSV, same dosage). Tumors developed at inoc. site in 7-13 days in all mice inj. i.m. and the large tumors were lethal to all mice. Dilute (1:10) MSV increased survival in the mice inoc. s.c. and i.m.; 30% of these mice died of lymphocytic leukemia with no observable solid tumor. Infectious MSV was found in the spleens, plasma and tumors of the animals. MSV tumor cells could not be cultured in vitro. Almost all mice inoc. with HSV died by day 50, with angiosarcoma-like tumors and hemorrhagic brain lesions. The HSV tumor cells were easily cultured in vitro.

70-1958 CARCINOGENESIS BY RNA SARCOMA VIRUSES. XIV. INFECTION OF STATIONARY CULTURES WITH MURINE SARCOMA VIRUS (HARVEY). (E.) Murray, R. K. (U. Toronto, Ontario, Canada) and H. M. Temin. Int. J. Cancer 5(3):320-326, 1970.

Stationary mouse embryo cell cultures (obtained by removal of serum) were exposed to the Harvey sarcoma virus (HSV) complex, but no focus-forming virus was produced. HSV production after cell division occurred when serum was added to these cultures. Cytosine arabinoside (CA; 5×10^{-5} M) inhibited virus production when added to stationary

cultures immediately after exposure to virus; inhibition by CA was prevented by deoxycytidine (1×10^{-4} M). These findings suggest that both cell division and non-S-phase DNA synthesis are required for production of this virus complex, and parallel the results obtained previously with the avian sarcoma complex.

70-1959 EVIDENCE FOR A FUNCTIONAL CHANGE IN THE PLASMA MEMBRANE OF MURINE SARCOMA VIRUS-INFECTED MOUSE EMBRYO CELLS. TRANSPORT AND TRANSPORT-ASSOCIATED PHOSPHORYLATION OF ^{14}C -2-DEOXY-D-GLUCOSE. (E.) Hatanaka, M. (Flow Labs. Inc., Rockville, Md.), C. Augl and R. V. Gilden. J. Biol. Chem. 245(4):714-717, 1970.

The uptake of ^{14}C -2-deoxy-D-glucose (10^{-2} - 10^{-6} M) by NIH Swiss mouse embryo fibroblasts at the time of transformation by the Harvey strain of mouse sarcoma virus proceeded at a greater rate, a lower K_m (2.5 - 5.0×10^{-4} M as compared to 21.0 - 23.3×10^{-4} M) and a higher V_{max} (52.3 - 83.5 $\mu\text{M}/\text{mg}$ protein/min. as compared to 18.2 - 19.2 $\mu\text{M}/\text{mg}$ protein/min.) than in uninfected cells. The intracellular isotope was mainly found as 2-deoxy-D-glucose 6-phosphate, but in uninfected cells, a larger percentage was 2-deoxy-D-glucose. The increased phosphorylation was not seen with cell homogenates and no increased hexokinase activity was found, indicating that the enhanced sugar uptake was due to alterations in the plasma membrane transport.

70-1960 THE IMMUNODEPRESSIVE EFFECT OF A MURINE PLASMODIUM AND ITS INTERACTION WITH MURINE ONCOGENIC VIRUSES. (E.) Salaman, M. H. (Roy. Coll. Surg., London), N. Wedderburn and L. J. Bruce-Chwatt. J. Gen. Microbiol. 59(3):383-391, 1969.

The immunologic response of 8-week-old BALB/c mice inj. with sheep RBC (2.5×10^8 cells, i.v.) was greatly depressed coincident with a high level of parasitemia induced by i.p. inj. of Plasmodium berghei yoelii (Pby). In 10-week-old BALB/c mice receiving 10^6 Pby cells i.v. and Harvey sarcoma virus 10 days later, the spleens weighed an av. of 0.71 g and had numerous superficial nodules after 4.5 weeks, as compared to a wt. of less than 0.25 g for spleens from those mice given virus alone. No solid tumors were seen in either group. BALB/c mice carrying a vertically-transmitted virus derived from urethan-induced leukemia were infected with Pby at 6-10 weeks of age, and instead of recovering from the malarial infection like normal mice, 16/19 died between days 15-21 with 50% or more parasitized RBC and gross anemia. These results are discussed in relation to malarial infection and development of Burkitt's lymphoma in children.

70-1961 CONTROL OF MULTIPLICATION OF UNINFECTED RAT CELLS AND RAT CELLS CONVERTED BY

URINE SARCOMA VIRUS. (E.) Temin, H. M. (U. Wisconsin McCardle Lab., Madison). J. Cell Physiol. 75(1):107-119, 1970.

direct relationship was found between the amount of serum added (human, horse or calf) and the uptake of ^3H -thymidine (due to increased number of cells) by fibroblast cultures of 14-16-day-old embryos from Sprague-Dawley rats. Insulin and nonsuppressible insulin-like activity- and -P also had multiplication-stimulating activity (msa; the capacity to stimulate DNA synthesis and cell division in stationary populations of cells). Uninfected rat-cell cultures are found to be continually producing msa with no inhibitory or toxic agents, while murine sarcoma virus (Harvey)-infected cells multiplied more than the uninfected cells with the same amount of serum and produced a toxin which nullified the effects of added calf serum. Although the efficiency of ^3H -thymidine uptake was similar, the infected cells demonstrated a greater efficiency of utilization of msa in the presence of serum.

0-1962 TEMPERATURE SENSITIVE MUTANTS OF AN AVIAN SARCOMA VIRUS. (E.) Toyoshima, T. (U. Washington Sch. Med., Seattle) and P. K. Ogst. Virology 39(4):930-931, 1969.

chick embryo fibroblasts were inoc. with 10^6 FFU of B77 virus, and on day 5, the transformed virus-producing cells were exposed to 5-azacytidine (25 $\mu\text{g}/\text{ml}$; at $36^\circ\text{C} \times 24$ hours). Mutagenized virus was then plated onto type C/0 chick embryo fibroblasts at the permissive temperature (36°C). Most of the virus clones produced had reduced focus-forming efficiency and yield at the non-permissive temperature (40.5°C), but 2 were strongly suppressed. No foci of transformed cells were observed in cultures incubated with the temperature-sensitive mutants at the non-permissive temperature, or shifted to non-permissive temperatures after 20 hours. Foci induced by the virus disappeared after shifting to non-permissive temperatures as late as 20 hours after infection. The temperature-sensitive mutants also could not replicate at the non-permissive temperature.

0-1963 CARCINOGENESIS BY RNA SARCOMA VIRUSES. XII. A QUANTITATIVE STUDY OF INFECTION OF RAT CELLS IN VITRO BY AVIAN SARCOMA VIRUSES. (E.) Altaner, C. (Cancer Res. Inst., Bratislava, Czechoslovakia) and H. M. Temin. Virology 30(1):118-134, 1970.

rat embryo fibroblasts infected with Bratislava 7 (B77) avian sarcoma virus developed foci of converted cells within 6-8 days; their number was linearly related to virus conc. Experiments were performed which demonstrated rat cells could be converted by single particles of the size, density and UV sensitivity of B77 virions and

that live cells, virus precursors and subunits were not necessary. Passage of the B77 virus through rat cells produced a genetically altered virus (RBA) with an increased plating efficiency on rat cells and a different antigenicity. Avian tumor viruses were subgrouped according to envelope type, which was not correlated with plating efficiency. Plating efficiency on rat cells was not much increased by treatment with inactivated Sendai virus. Inj. of 10^4 converted cells s.c. into newborn Sprague-Dawley rats induced tumors in 2/4.

70-1964 EXPERIMENTAL INDUCTION OF LYMPHOSARCOMA IN THE CAT WITH "C"-TYPE VIRUS. (E.) Theilen, G. H. (U. California Sch. Vet. Med., Davis), D. L. Dungworth, T. G. Kawakami, R. J. Munn, J. M. Ward and J. B. Harrold. Cancer Res. 30(2):401-408, 1970.

Whole-cell suspensions (5 ml) or cell-free material from a 3-yr.-old Persian cat that had died from lymphosarcoma were inj. i.p. into 9 domestic short-hair kittens, 1-4 days old. All the kittens died within 11 weeks, and all except 1 had a variety of clinical signs. Definite lesions of lymphosarcoma were seen in 5/8, possible early changes in 2 and no gross or histological signs in 1. Mature and immature virus-like Type C particles, previously seen in the donor, were observed in the 5 kittens with definite signs of lymphosarcoma and more easily in those inoc. with cell-free material.

70-1965 FELINE LEUKEMIA AND SARCOMA VIRUSES: SUSCEPTIBILITY OF HUMAN CELLS TO INFECTION. (E.) Sarma, P. S. (NCI, Bethesda, Md.), R. J. Huebner, J. F. Basker, L. Vernon and R. V. Gilden. Science 168(3935):1098-1100, 1970.

Feline sarcoma virus (FSV; derived from a 5.5-yr.-old Siamese cat with naturally-occurring fibrosarcoma) and feline leukemia virus (FeLV; purified tumor concentrate or grown in feline embryonic fibroblast culture were inoc. into human cells (embryonic fibroblasts) in culture. The cells remained normal when infected with FeLV, but FSV resulted in cell transformation by day 15 after virus inoc., with C-type particles seen by day 6. Further, FSV and FeLV grown in human cultures were infectious for feline, canine and human embryo cultures. Human cells were 10-fold less susceptible than feline cells to FSV. The possibility of in vivo susceptibility of human cells to FeLV is suggested, as well as a theory to associate FSV and FeLV with human cancer.

70-1966 AN IMMUNOLOGICAL EXPLANATION FOR THE STARRY SKY HISTOLOGICAL PATTERN OF A MALIGNANT LYMPHOMA. (E.) Sinkovics, J. G. (U. Texas M. D. Anderson Hosp. Tumor Inst., Houston), R. J. Pienta, J. M. Trujillo and M. J. Ahearn. J. Infect. Dis. 120(2):250-254, 1969.

Histological section of a murine lymphosarcoma revealed abundant macrophages phagocytizing lymphoid cells. Leukemia virus particles and globulin molecules were both found in cultured lymphoblasts. Lymphoblast growth was not suppressed by immune lymphocytes *in vivo* but was suppressed by macrophages. It is postulated that the viral neoantigens on the cell surface are coated with specific globulins produced by the same cell that manufactures the viral neoantigens; thus, these globulins may be regarded as self-enhancing antibodies allowing the lymphoma cells to present with antigenically 'self' surface properties. Immune lymphoid cells failed to significantly suppress lymphoma cell growth *in vivo* because they cannot recognize neoantigenic sites coated with host-type globulins. Macrophages readily phagocytized opsonized antigens, indicating a failure of the globulin coat to protect the neoantigenic cells. The "starry sky" histological pattern signifies antibody-coated neoantigenic sites on the lymphoma cells; these sites are recognized as opsonized antigens by macrophages, resulting in lymphoma cell phagocytosis.

70-1967 INFLUENCE OF BOVINE LEUKEMIA ON THE OCCURRENCE OF NEOPLASTIC DISEASES IN MAN BASED ON MATERIAL COLLECTED IN THE DISTRICT OF ZLOTOW. (Pol.) Muszyński, B. Przegl. Lek. 15(9):660-661, 1969.

A 55-yr.-old man developed lymph node tumors several mo. after a neighbor's cow was reported as having leukemia. Also, a 15-yr.-old boy with lymphosarcoma of 2-yr. duration lived within a 0.5-1.0 km range of 3 different sources of confirmed leukemia in cattle. An increased frequency of tumor (2 cases of Hodgkin's disease, 1 lymphoreticulosarcoma during the first 3 mo. of 1968, as compared to 3 cases in all of 1966) was seen in the same district (Zlatow, Poland) where in 1967 leukemia, leukocytosis (8000-45,000 WBC, with 70-89% lymphocytes) and a normal blood picture were seen in 4, 16 and 88/167 cattle, resp., examined and found free of brucellosis or tuberculosis. It is suggested that increased frequency of leukemia among men and cattle is more than coincidental, and a study of the possible relationship between the two is recommended.

70-1968 TRANSFER RNA'S IN HUMAN LEUKEMIA. (E.) Gallo, R. C. (NCI, Bethesda, Md.). J. Cell Physiol. 74(2, Pt. 2):149-153, 1969.

Transfer RNA in lymphoblasts from normal persons and from pts. with acute or chronic lymphocytic leukemia were compared by cochromatography after acylation with ^3H - or ^{14}C -labeled amino acids. The lymphoblasts were morphologically identical, had identical generation times (about 30 hours) and were obtained in midphase of log growth. Elution profiles of isoleucyl-, tyrosyl-,

leucyl-, and arginyl-transfer RNA are presented as examples.

70-1969 IMMUNOLOGICAL STUDIES ON LEUKEMIA WITH SPECIAL REFERENCE TO THE CIRCULATING ANTIBODIES AGAINST THE HUMAN LEUKEMIC ANTIGENS IN HUMAN SERA. (E.) Kamiya, H. (Mie Prefect. U. Sch. Med., Tsu, Japan). Mie Med. J. 29(2): 157-171, 1969.

Specific antisera to leukemic WBC and leukemic brain tissue were prepared in rabbits and confirmed by the passive cutaneous anaphylaxis and immune adherence tests. Tests for circulating leukemia antigen in the sera of 204 persons (including 54 with leukemia, 25 with leukemia analogous disease and 102 members of their families) by passive cutaneous anaphylaxis showed positive reactions in 25% in the families of those with leukemia analogous disease, 8.7% of the pts. with leukemia analogous disease, 2.6% in the families of leukemic pts. and none of the leukemic pts. Using the immune adherence test, various results were obtained with different leukemic antigens, but no significant circulating antibody was found in any of the leukemic families.

70-1970 PARTIAL FAILURE OF METHYLATION AND CLEAVAGE OF 45S RNA IN THE BLAST CELLS OF ACUTE LEUKAEMIA. (E.) Torelli, U. L. (U. Modena Inst. Med. Path., Italy), G. M. Torelli, A. Andreoli and C. Mauri. Nature (London) 226(5251):1163-1165, 1970.

Homogeneous blast cells from 6 pts. with forms of acute leukemia (2 lymphoblastic, 1 monocytic, 3 myeloblastic) and with WBC counts from 35,000-90,000/mm³ were cultured with labeled RNA precursors and the sedimentation patterns were characterized. Similar results were seen for all forms of leukemia. For short incubation periods (30-60 min.) with ^3H -uridine, all cases exhibited normal blast cell synthesis of ribosomal precursor RNA. For a 6-hour incubation time, radioactive label was associated with the 30S-50S RNA region, peaking at 45S, rather than at 18S or 28S RNA. Results for ^3H -methionine confirmed ribosomal RNA synthesis, but showed an increase in radioactivity at the 18S and 28S-32S peaks with a proportionate decrease for the 45S fraction. It is concluded that in the blast cells of acute leukemia, undermethylated 45S and 32S RNA accumulates and there is reduced cleavage of 45S RNA.

70-1971 SUPPRESSION OF ESTABLISHED FRIEND VIRUS LEUKEMIA BY STATOLON. I. DEMONSTRATION OF A LATENT INFECTION IN CLINICALLY NORMAL MICE. (E.) Wheelock, E. F. (Case Western Reserve U. Sch. Med., Cleveland, Ohio), N. L. Caroline and R. D. Moore. J. Virol. 4(1):1-6, 1969.

BA/2 mice with established Friend virus (FV) leukemia received statolon (S; 4 mg/mouse, i.v.) 5 days after FV inoc. and subsequently had a clinical remission lasting several mo. More than 50% of those mice appearing normal at 78 days post-FV inoc. developed leukemia and died within the next 240 days. Cell transfer experiments were used to demonstrate FV activity in the spleens of virus-infected S-treated mice. Transfer of 10^7 spleen cells from mice in remission to normal mice produced FV leukemia. Three clinically normal S-treated mice were rechallenged with FV and after 21 days showed normal spleens and livers compared to challenge controls. Spleens from S-protected mice contained aggregates of abnormal FV leukemia-like cells directly beneath the capsules. This long-term protection against FV leukemia is probably maintained by an immunologic mechanism which is mobilized in some mice under the cover of interferon (I). Therefore, S may contain in addition to the I-inducing double-stranded RNA, a substance which stimulates an immunologic response to FV.

70-1972 EFFECTS OF FRIEND LEUKEMIA VIRUS ON THE IMMUNE RESPONSE OF MICE TO BACTERIAL ANTIGENS. (E.) Flickinger, J. T. (Univ. Hospital Ctr., Sherbrooke, Quebec, Canada) and J. M. Gentile. Canad. J. Microbiol. 16(8): 741-745, 1970.

Bacterial antigens prepared from Salmonella typhimurium or Proteus mirabilis were inj. i.p. 1-5 days before injecting female, 8-10-week-old BALB/c mice were inj. with 20 FFU Friend leukemia virus (FLV) i.v. The longer the interval between the 2 inj. the more normal was the response to the bacterial antigens; the only significant difference was a suppression of anti-response when the antigen was inj. 1 day before FLV. Animals sensitized with bacterial antigen simultaneously or 1-5 days after FLV inoc., had a suppressed immunologic reaction to both O and H antigens, the latter being more pronounced. The presence of O and H antigen together did not alter the pattern of immunosuppression.

70-1973 USE OF INTERFERENCE PHENOMENA FOR DETECTION OF SOME MOUSE LEUKEMIA VIRUSES IN TISSUE CULTURE. (Rus.) Merekalova, I. (Inst. Exp. Clin. Oncol., Moscow). Biull. Sp. Biol. Med. 74(7):74-76, 1969.

The possible interference between some infectious viruses and Friend leukemia viruses (FLV) or Moloney leukemia viruses (MLV) was studied in cultures of embryonic fibroblasts of strain BALB/c and CC57Br mice. In the fibroblasts infected with FLV and then with mouse encephalomyelitis virus (EMV), both experimental and control cultures showed cytopathic effects of the same intensity and at the same time. The

dose of EMV was decreased and an interference was noted between FLV and EMV in 11/14 experiments. Neutralization experiments with FLV immune sera (IS) showed that tissue cultures treated with FLV + IS acted toward EMV almost as did noninfected cultures. Some experiments showed very slight inhibition of cytopathic effects of EMV, apparently due to the nonspecific action of the serum. In the cultures treated with FLV + normal serum, interference was the same as in cultures infected with FLV alone. It is concluded that the serum neutralized FLV and interference with EMV was absent. In cultures infected with MLV and then EMV, interference phenomena were absent. Both FLV and MLV showed very slight interference with smallpox vaccine. It is suggested that the interference phenomenon could be used as an indirect method for detecting FLV in tissue culture.

70-1974 SPLEEN FOCI AND POLYCYTHEMIA IN C57BL MICE INFECTED WITH HOST-ADAPTED FRIEND LEUKEMIA VIRUS. (E.) Steeves, R. A. (Roswell Park Mem. Inst., Buffalo, N. Y.), E. A. Mirand, A. Bulba and P. J. Trudel. Int. J. Cancer 5(3):346-356, 1970.

Passage in newborn C57BL mice markedly altered the host range of Friend leukemia virus (FLV). BSB and BB6, virus isolates from the original FLV, gave "Friend disease" and polycythemia in suckling or adult C57BL mice. Both differed from the parent virus in Swiss mice by their longer latent period and lower mortality in adult C57BL mice. The replication of spleen focus-forming virus (SFFV) from BSB or BB6 was limited in suckling mice and almost nonexistent in adult C57BL mice. The host susceptibility to SFFV in BSB isolate varied according to age in young adult C57BL mice, and was affected by a gene closely linked with or at the histocompatibility-2 locus. In adult BALB/c mice spleen focus formation by either isolate yielded 1-hit dose-response relationships, in contrast to the multiple-hit relationship obtained with the parent virus. With this virus-host system, there was an association between virus replication and virulence of the induced disease, and also an association between adaptation of SFFV to the C57BL strain and an increased conc. of either competent virions or helper virus.

70-1975 HOST-INDUCED CHANGES IN INFECTIVITY OF FRIEND SPLEEN FOCUS-FORMING VIRUS. (E.) Steeves, R. A. (Roswell Park Mem. Inst., Buffalo, N. Y.) and R. J. Eckner. J. Nat. Cancer Inst. 44(3):587-594, 1970.

Spleen focus-forming virus (SFFV-S) maintained in Swiss mice was passaged 3 times through newborn BALB/c mice and the recovered virus, designated SFFV-B, differed in host range from SFFV-S, as determined by the spleen focus assay method. No antigenic differences were detected

between SFFV-B and SFFV-S when compared by their neutralization kinetics with rabbit antisera against normal Swiss or BALB/c tissue. Titration of SFFV-S in BALB/c mice gave a multiple-hit, dose-response curve, but titration of SFFV-B in BALB/c mice and of SFFV-S in Swiss mice gave 1-hit, dose-response relationships. SFFV-S yielded a 1-hit, dose-response curve in BALB/c mice coinfecting with a lymphatic leukemia virus (LLV-S) isolated in Swiss mice from Friend virus complex and free of detectable SFFV. The passage of LLV-S through newborn BALB/c mice gave virus (LLV-B) with a markedly increased helper activity. It is concluded that SFFV, as expressed in BALB/c mice, is defective, because an associated virus particle, LLV, is necessary in addition to SFFV for spleen focus formation.

70-1976 THE PASSIVE IMMUNOTHERAPY OF MURINE LEUKAEMIA. I. THE PRODUCTION OF ANTISERA AGAINST LEUKAEMIC ANTIGENS. (E.) Motta, R. (Paul Brousse Hosp. Inst. Cancer Immunogenet., Villejuif, France). Rev. Europ. Etud. Clin. Biol. 15(2):161-167, 1970.

Groups of 8-10-week-old male C57BL/6 mice, CF rats or Bourgogne rabbits were immunized with splenic cells from normal DBA/2 mice or from DBA/2 mice treated with leukemic spleen cells induced by Friend leukemia virus. These cells were inj. along with host antisera against normal DBA/2 spleen cells, normal host sera, or Tyrode medium alone. Passive administration of anti-normal cell antiserum permitted the development of antibodies directed almost exclusively against the leukemic antigen. Antibodies produced against tumor associated antigen were increased in mice and rabbits. Generally, a higher cytotoxic activity was seen in groups receiving living cells.

70-1977 POWERFUL NEW INHIBITOR OF MURINE LEUKAEMIA AND SARCOMA VIRUSES. (E.) Chermann, J. C. (Pasteur Inst., Garches, France), M. Raynaud, C. Jasmin and G. Mathé. Nature (London) 227(5254):173-174, 1970.

Adult BALB/c mice inoc. with Friend leukemia virus (FLV) were admin. an inhibitor prepared from silicotungstic acid supernatants of cell cultures or mouse spleens (STAS; 0.01-5 mg/mouse, i.p.) and spleen wt. determined after 3 weeks. Rauscher leukemia virus from the JLSV5 cell line and STAS inhibitor were admin. i.p. to newborn BALB/c mice which were examined in 45 days. STAS and Moloney sarcoma virus (MSV) were admin. i.m. to newborn C3H mice and tumor development observed. STAS (1 mg) inj. simultaneously with FLV resulted in almost complete inhibition of leukemia; when inj. after 8 days it was inactive. STAS also inhibited muscle tumor formation in MSV-inoc. mice, especially STAS from the JLSV5 cell line. In studies of cell transformation in vitro with MSV and STAS (1 mg) in secondary

mouse fibroblasts, the JLSV5 culture STAS caused complete inhibition. It is concluded that the inhibitor isolated by STAS is not an antigenic part of the virus surface, a mouse antiviral antibody, or an interferon; rather, by some mechanism its absence enhances virus potency.

70-1978 INHIBITION OF PHYTOHEMAGGLUTININ- AND ALLOANTIGEN-INDUCED LYMPHOCYTE STIMULATION BY RAUSCHER LEUKEMIA VIRUS. (E.) Häyry, P. (U. Helsinki), D. Rago and V. Defendi. J. Nat. Cancer Inst. 44(6):1311-1319, 1970.

BALB/c mice were inoc. with Rauscher leukemia virus (RLV; 0.1 ml, i.p.) and examined in vitro for spleen, lymph node cell and peripheral blood lymphocyte (PBL) response to phytohemagglutinin (PHA)- and alloantigen-induced stimulation. Results showed PHA stimulation of spleen cells to progressively decrease (84% and 5% the value of controls on days 1 and 60, resp.); these effects were evident well before any specific histologic or other signs of leukemia. Response of lymph node cells or PBL did not differ from controls. The pattern of response for allogeneic stimulation of lymph node cells resembled that of PHA; however, this response decreased by week 4 after RLV inoc., but did not decrease with PBL in the experimental group during the 28 days of observation. Lymphocytes from normal BALB/c mice exposed to RLV in vitro had decreased response to PHA and allogeneic lymphocytes, thus demonstrating that immunodepression in the infected animals was produced by a direct effect of the virus on the lymphoid cells. It is concluded that RLV-induced depression of cell-bound immunity should be considered in the pathogenesis of viral leukemia.

70-1979 EXCRETION OF MURINE LEUKAEMIA VIRUS. (E.) Myers, D. D. (Jackson Lab., Bar Harbor, Me.), H. Meier, J. S. Rhim and R. J. Huebner. Nature (London) 226(5248):849-850, 1970.

Excretion of an unspecified murine leukemia virus (MLV) in 6-10-mo.-old, high leukemia strain mice was studied. MLV was isolated from 4/44 fecal and 6/44 blood specimens of AKR/J mice. Also, MLV was isolated from 3/36 and 0/24 blood specimens from C58/J and SJL/J mice, resp. It is concluded that virus transmission is vertical, as a covert viral genome, and that the appearance of excreted virus may indicate a defense mechanism rather than a mode of viral spread.

70-1980 ANTIGENIC PROPERTIES OF A NONRELEASER NEOPLASM INDUCED IN THE MOUSE BY MURINE SARCOMA VIRUS. (E.) Law, L. W. (NCI, Bethesda, Md.) and R. C. Ting. J. Nat. Cancer Inst. 44(3):615-621, 1970.

eudotype virus-specific antigenicity was found in a nonreleaser neoplasm, a hemangiosarcoma induced by the pseudotype virus of a rat-adapted strain of murine sarcoma virus (MSV-33, derived from Rauscher leukemia virus) which bore the envelope of the Moloney leukemia virus (MLV). V was used as a "helper" virus to rescue this eudotype virus. A nonreleaser neoplasm, XM-1 induced by MSV-33 in a (C57BL x C3H)F₁ mouse), was selected by passage through immunologically deficient syngeneic, BC3HF₁ mice. Results support the hypothesis that virus-specific cell surface antigens exist on RNA virus-induced cancers, and that these antigens are distinct from the viral antigens. A direct relationship between viral genetic material maintained in the cancer cells and the presence of tumor-specific transplantation antigens is also suggested.

-1981 FORMATION OF VIRUS-LIKE PARTICLES BY BONE CELLS IN MICE WITH A HIGH INCIDENCE OF SPONTANEOUS LEUKEMIA. (E.) Schofield, H. (Johns Hopkins Hosp., Baltimore, Md.), P. Barrett, S. B. Doty, F. H. J. Figge and A. Robinson. Science 168(3931):588-589, 1970.

bone marrow samples from 3-36-week-old AKR and C3H/Fg male mice (80-90% spontaneous leukemia incidence) were examined and all mice were found to have leukemogenic viruses (MLV) identical to particles previously found in lymphopoietic tissues from potentially leukemic and leukemic mice. More particles were associated with osteocytes than osteoblasts; they appeared to originate from both cell types by budding from plasma membranes. Although present in small numbers in normal mice, large numbers of particles were not observed in lymphopoietic tissues except in terminally leukemic mice. No particles were observed in bone or lymphopoietic tissues from 4 strains of mice having a low incidence of leukemia.

-1982 NON-LEUKAEMIC AKR MICE ARE NOT TOLERANT TO CELLS OF LEUKAEMIA INDUCED BY GROSS VIRUS. (E.) Doré, J. F. (Paul Brousse Hosp. St. Cancer Immunogenet., Villejuif, France), E. Auria and G. Mathé. Rev. Europ. Etud. Clin. Oncol. 15(1):81-84, 1970.

The mortality of 2-mo.-old female AKR mice increased as the number of leukemic cells (K36, spontaneous AKR leukemia; 10^2 - 10^7 cells) injected increased. A lower mortality was observed when cells were injected s.c., as opposed to i.v. or p., when the mice were treated before and after injection of K36 cells with B.C.G. or dead *Corynebacterium parvum*, or when the mice were immunized s.c. with E δ G₂ leukemia cells (induced in 7BL/6 mice by the Gross virus). Immune adherence activity was seen against K36 cells in AKR mice treated with B.C.G. and/or immunized with E δ G₂ leukemia cells; cytotoxic activity against K36 cells, against leukemic cells induced

in C3H/Jax mice by Gross virus and against cells from a spontaneous AKR leukemia was seen in mice receiving a prolonged immunization with K36 cells. This evidence opposes the idea that AKR mice are more tolerant to leukemic cells induced by the Gross virus.

70-1983 GENETIC BASIS FOR SUSCEPTIBILITY TO LEUKEMIA INDUCTION BY AKR THYMUS GRAFTS. (E.) Nakakuki, K. (Mie Prefect. U. Sch. Med., Tsu, Japan). Gann 61(1):85-87, 1970.

Male and female hybrid mice, strains (C3Hf x AKR)F₁ and (C57BL x AKR)F₁, received thymus transplants from AKR mice (5 mo. old, nonleukemic) and C3Hf and C57BL mice (5-6 mo. old). Also, AKR mice (25-30 days old) received transplants from 5-mo.-old AKR mice. By 180 days, 17/22 (77.3%) AKR mice developed leukemia, as did 23/34 (67.6%) (C3Hf x AKR)F₁ hybrid mice. No C57BL hybrid mice developed leukemia by 180 days. Leukemias were lymphomas, with enlargement of host thymus and of some grafted thymus. Secondary transplants from the leukemic hybrid mice resulted in leukemia of similar mice only. It is suggested that the presence of a large quantity of Gross leukemia virus in AKR mice, as well as the above hybrid strains, indicates the leukemogenic nature of AKR thymus grafts and an associated viral mechanism.

70-1984 BIOLOGICAL AND MORPHOLOGICAL STUDIES OF SJL/J STRAIN RETICULUM CELL NEOPLASMS INDUCED AND TRANSMITTED SERIALLY IN LOW-LEUKEMIA-STRAIN MICE. (E.) Fujinaga, S. (U. Texas M. D. Anderson Hosp. Tumor Inst., Houston), W. E. Poel, W. C. Williams and L. Dmochowski. Cancer Res. 30(3):729-742, 1970.

Extracts of tissues of SJL/J mice (12-14 mo. old) with reticulum cell sarcoma were injected into 1-14-day-old BALB/c mice (0.2 ml filtrate, i.p.) and reticulum cell neoplasms (RCN) developed in 4/34 mice. Serial transmission to other low-leukemia strains (BALB/c, C3H/f and C3HeB/FeJ) induced Type A and B RCN and heterotopic myelopoiesis (possibly myeloid or erythroid leukemia). With increased number of transmissions, tumors increased to 92% frequency and the latent period decreased. The virus particles were of the structure of C-type mouse leukemia virus and similar to virus particles of cultures of tumorous spleen from SJL/J mice with spontaneous RCN. Virus produced in the tumorous spleen cultures was biologically active in BALB/c mice. A viral etiology of RCN is suggested by the similarities of particles from leukemic mice and mice with spontaneous neoplasms.

70-1985 ANIMAL EXPERIMENTAL STUDIES OF THE REISOLATION OF MYELOID LEUKEMIA VIRUS (GRAFFI ET AL.) IN THE MOUSE. (Ger.) Fey, F. (Inst. Cancer Res., Berlin). Folia Haemat. (Leipzig) 91(2-3):245-252, 1969.

Filtrates of mouse leukemia cells were inj. s.c. into newborn XVII mice, 5, 10 or 20 days prior to sacrifice and s.c. inj. of cell-free organ filtrates into newborn hosts of the same strain. Myeloid leukemia cells induced significant leukemogenic activity in the spleen, liver, lymph nodes, bone marrow and thymus (but not in the brain) at 5 days, with the liver and spleen predominating. Activity in all the organs studied was max. at 10 days. Paramyeloblastic leukemia cells induced significant activity in the spleen alone at 5 d; a high degree of activity in the spleen, liver, thymus and bone marrow at 10 days. Activity in all organs was max. at 20 days. Lymphatic leukemia cells induced significant activity in the thymus alone at 5 days, with some activity demonstrable in the spleen and bone marrow. Activity in all organs was max. at 10 days, with the thymus, liver and lymph nodes predominating. For reticular leukemia cells at 10 days, significant activity was seen in the thymus alone, which reached max. activity at 20 days, accompanied by moderate activity in the spleen, liver and lymph nodes. When the mice were splenectomized 1-6 days after infection, myeloid leukemia takes were reduced from 89% to 22%, and reticular leukemia takes from 70% to 46%.

70-1986 THE IN VITRO CULTURE OF MOUSE MYELOID LEUKEMIA VIRUS (GRAFFI ET AL.). (Ger.) Schramm, T. (Inst. Cancer Res., Berlin). Folia Haemat. (Leipzig) 91(2-3):260-265, 1969.

After infection with mouse myeloid leukemia virus, viral replication for at least 3 mo. was obtained in 43.5% of cultures made from whole mouse embryo and 85.3% of those made from mouse spleen. Successful induction of leukemia followed s.c. inoc. into newborn XVII, CBA, C57BL and AB mice of the culture medium (19.5%), ultrasediment from the culture medium (42.3%), viable cells from the culture medium (30.0%) or cells which were frozen and thawed at a later (unspecified) date (56.9%). Induced leukemias included myeloid (60.4%, of which 60.4% were chloroleukemias), myeloid-reticular (11.9%), reticular (4.4%), reticular-lymphatic (3.1%), lymphatic (3.8%), paramyeloid (5.0%) and erythroblastic (2.5%), with 8.8% of the animals developing thymomas. In correlative studies, the percentages of cultures achieved, in terms of cell population employed (mean latency times in inoc. animals in parentheses), were as follows: HeLa, 45.3% (157.5 days); whole rat embryo, 31.5% (317.7 days); calf kidney, 10.6% (473.6 days); and human embryonic kidney, 9.3% (512.3 days).

70-1987 VIRUS INDUCED ANTIGENS IN THE PRE-LEUKEMIC STAGE OF MYELOID LEUKEMIA IN THE MOUSE. (Ger.) Pasternak, G. (Inst. Cancer Res., Berlin). Folia Haemat. (Leipzig) 91(2-3):266-269, 1969.

Virus-induced antigens could not be demonstrated in the spleens of newborn mice 14 days after inj. with an unspecified leukemia virus. No significant amounts of such antigen was found in the liver, brain, thymus or lymph nodes 100 days postinfection.

70-1988 LEUKEMIA VIRUSES ASSOCIATED WITH MOUSE MYELOMA CELLS. (E.) Watson, J. (Salk Inst. Biol. Studies, San Diego, Calif.), P. Ralph, S. Sarkar and M. Cohn. Proc. Nat. Acad. Sci. USA 66(2):344-351, 1970.

Myeloma cells derived from C3H and BALB/c mice were cultured and analyzed for evidence of virus. An RNA-containing virus with RNA with a sedimentation coefficient of 74S and a base composition similar to some murine leukemia and sarcoma viruses was found. Extra- and intracellular virus particles of density 1.20-1.22 g/cm³ and 1.29-1.33 g/cm³, resp., were found containing the leukemia virus group-specific antigen. Direct cytotoxicity tests showed almost all cells were Gross leukemia-positive. Infectivity of the virus in vitro or in vivo could not be seen.

70-1989 MATURATION OF MYELOID CELLS IN VIRUS-INDUCED CHLOROLEUKEMIA IN THE MOUSE, PASSED BY CELL TRANSPLANTS. (Ger.) Fritsch, S. (Inst. Microbiol. Exp. Ther., Jena, Germany). Folia Haemat. (Leipzig) 91(2-3):270-276, 1969.

Chloroleukemia was induced in newborn, inbred Agnes Blum/Jena mice by inj. of cell-free filtrates of ascites sarcoma RAB 1, and was then maintained in 2 lines through 17 passages by s.c. and i.p. cell transplants, resp. In both lines, as the number of passages increased, an increasing tendency of the leukemic cells to cease maturation at the promyelocyte stage was seen. Even in the early passages, electron microscopic study showed a disturbance of granular formation, with both excessive and diminished amounts of peroxidase granules/cell and with frequent occurrence of cells with no peroxidase granules. This was accompanied by hyperplasia of the Golgi apparatus and asynchronous maturation of the nucleus and cytoplasm. As the number of passages increased, the occurrence of cells with diminished or no peroxidase granulation also increased markedly, as did the occurrence of myeloblastic transformations.

70-1990 VIRUS PARTICLES IN RAT LEUKEMIAS. (E.) Chopra, H. C. (Charles Pfizer Co. Smith Mem. Cancer Res., Maywood, N. J.), N. J. Woodside and A. E. Bogden. Cancer Res. 30(5):1544-1547, 1970.

Thin section electron microscopy of transplantable lymphocytic, monocytic and chronic myelogenous leukemias in rats revealed Type C virus particles,

particularly in the lymphocytic leukemia. The mu particles were seen in the endoplasmic reticulum cisternae of tumor tissue, spleen, bone marrow, thymus and lymph nodes. Some extracellular virus particles, 100 mu in size, were found in transplantable tumor tissue and bone marrow of monocytic and myelogenous leukemia. Whether these Type C particles are actual biological agents or contaminants cannot be definitely concluded.

1991 LUNG TUMOR-BEARING STRAIN A MICE WITH COINCIDENT LEUKEMIA: AN ELECTRON MICROSCOPIC STUDY. (E.) Brooks, R. E. (U. Oregon Med. Sch., Portland). Cancer Res. 30(5):134-1540, 1970.

A group of strain A mice, 2 were found to have coincident lung adenoma and leukemia; 1 had been admin. urethan (U; 1% in the drinking water 24 days at age 3 mo.) and the other was a control. Examination of organs revealed a greatly swollen thymus, spleen and liver in both mice, but lymph nodes were not enlarged. Type C mouse leukemia virus particles were found in extracellular thymus and spleen. The lungs of U-treated animal showed Type A-2 particles in the tumor cells and Type C particles extracellularly, whereas no virus particles were seen in the lungs of the untreated mouse. The leukemia virus particles seen in the lung tumor cells are not considered to be related to the etiology of lung adenoma; the U is also not implicated in this respect. It is suggested, however, that the lung adenoma cells are susceptible to viral infection.

1992 LEUKEMIA AFTER TRANSPLANTATION OF RENAL OR PULMONARY TISSUE IN C57BL MICE. (E.) Rudali, G. (Radium Inst. Genet. Lab., Paris), P. Jullien and C. Silberman. Nouv. Rev. Franc. Hemat. 9(6):783-794, 1969.

In C57BL mice, transplantation of isologous kidney or lung tissue of very old XVII/G mice produced lymphatic leukemias at a high frequency (34% for kidney, 70% for lung); implantation s.c. of small kidney pieces of old XVII/G mice produced leukemia in 25%, whereas tissue transplants of newborn mice were completely ineffective. The induced leukemias were "superinfecting" for AKR mice. Extracts of normal lymph organs from very young C57BL mice did not induce leukemia, but the activity was acquired after passage 4; however, C57BL mice were sensitive to the Graffi virus while XVII/G mice were resistant. Implantation s.c. of inert materials (glass, lead or plastic) did not induce development of leukemia.

1993 PRIMARY ANTIBODY RESPONSE IN MICE BEARING LEUKEMIA L1210. (E.) Bonmassar, E. (Microbiol. Assoc. Inc., Bethesda, Md.), A. Bonmassar, S. Vadlamudi and A. Goldin. Experientia 26(5):529-531, 1970.

The primary humoral antibody response was studied using the direct plaque-forming cell (PFC) method in male CDF₁ leukemic mice (L1210) immunized with sheep RBC (SRBC) 2, 3, 4 or 5 days after tumor transplantation. Sacrifice occurred 2, 4 or 6 days after immunization. Results showed PFC response to be higher on days 4 and 6 after inj. of SRBC in leukemic mice immunized 2 or 3 days after tumor transplantation than in nonleukemic mice. Leukemic mice, however, immunized 4 or 5 days after transplantation showed impaired PFC response on day 4 after SRBC inj.; thus, the influence of leukemic development on the primary antibody response was evidenced by a critical change 3-4 days after tumor transplantation. These findings indicate that leukemic growth did not depress the antibody response in mice immunized within 3 days after transplantation. The PFC kinetic pattern in leukemic mice indicates that growth of L1210 leukemia does not depress the primary humoral antibody response of the host unless the antigenic stimulus is given at a later stage of tumor development. Under such conditions, immunosuppression was observed 4 days after antigen admin.

1970-1994 MESOTHELIOMAS OF PERITONEUM, EPICARDIUM, AND PERICARDIUM INDUCED BY STRAIN MC29 AVIAN LEUKOSIS VIRUS. (E.) Chabot, J. F. (Duke U. Med. Ctr., Durham, N. C.), D. Beard, A. J. Langlois and J. W. Beard. Cancer Res. 30(5):1287-1308, 1970.

Strain MC29 avian leukosis virus grown in chick embryo cell cultures was inj. into the peritoneal, pericardial and air sac cavities and wing webs of 1-day-old white Leghorn chicks. Mesotheliomas developed in 52/148 (35%) birds inoc. i.p., with appearance of tumor related directly to dose (number of virus particles). Tumors appeared in 4/19 and 1/19 chicks receiving pericardial and wing web inj., resp. No fibrosarcomas developed despite MC29 alteration of embryonic cells. Peritoneal tumors were characterized by nodules in mesenteric folds, appearing in extreme numbers on the pancreas, although none were on the surface of the liver, spleen or kidney. Aberrant growth of cartilage was also seen. Epicardial and pericardial tumor growth was papillomatous, occurring in sheets or masses with cartilage nodules and invasion of cardiac muscle. These tissues, however, were altered far less than the peritoneum. It is concluded that MC29 virus influences the metaplastic potential of mesothelial cells.

1970-1995 CHROMATOGRAPHIC DIFFERENCES BETWEEN LYSYL-tRNA'S FROM AVIAN TUMOR VIRUS BAI STRAIN A AND VIRUS TRANSFORMED CELLS. (E.) Trávníček, M. (Inst. Organ. Chem. Biochem., Prague) and J. Říman. Biochim. Biophys. Acta 199(1):283-285, 1970.

BAL strain A virus and virus-transformed leukemic myeloblasts were isolated from the blood of leukemic chicks. Samples of transfer RNA (tRNA) were prepared and purified by Sephadex column chromatography. Aminoacyl-tRNA (lysyl and arginyl forms) of virus and transformed cells was run on methylated albumin kieselguhr columns. Large differences were observed between viral and cellular lysyl-tRNA. The viral form eluted as a single component, whereas the virus-transformed cells exhibited 2 components. No difference was seen between lysyl-tRNA from leukemia myeloblasts and liver of healthy chicks, and there was no difference between arginyl-tRNA of either viral or cellular origin.

70-1996 LIGHT AND ELECTRON MICROSCOPIC STUDIES OF A TRANSPLANTABLE MELANOMA ASSOCIATED WITH VIRUS-LIKE PARTICLES. (E.) Epstein, W. L. (U. California San Francisco Med. Ctr.) and K. Fukuyama. Cancer Res. 30(5):1241-1247, 1970.

Light and electron microscopic examination of a transplantable pigmented hamster melanoma which was transplanted s.c. through 15-52 generations revealed a rapidly growing, heavily pigmented melanoma with a constant association with virus-like particles (VLP). Malignant cells formed Fontana-positive pigment and grew as a solid tumor about dilated vascular channels with a supporting reticulum. No inflammatory response occurred, although necrosis and hemorrhage were prevalent. Stains for tyrosinase and acid phosphatase indicated that most viable cells contained both activities. There was a widespread presence of autophagosomes, containing primarily melanosomes in various stages of melanization and myelin figures. VLP were observed in the rough endoplasmic reticulum (RER) in a majority of cells of every generation of tumor; they did not occur in inflammatory or endothelial cells, or in surrounding normal structures. In albino hamsters the tumor grew more slowly, did not lose pigment and also had many VLP. The nature and source of VLP which abound in the RER of almost every melanoma cell are uncertain. It is suggested that these VLP may act to transform cells and increase their growth rate. Morphologically, the VLP corresponded most closely to the Type C body (Bernhard and Granboulan classification), and resembled particles of a small, coated RNA virus.

70-1997 INDUCTION OF CANCER IN MAMMARY ISO-GRAFTS FROM MALE DONORS TO CBA FEMALE HOST MICE. (E.) Hoshino, K. (U. Western Ontario Health Sci. Ctr., London, Canada). J. Nat. Cancer Inst. 44(4):819-825, 1970.

Mammary segments (106, each 0.6 mm long) with little surrounding adipose tissue from normal adult male CBA mice (milk-agent-positive) were transplanted to mammary-gland-free fat pads of the 1-7-mo.-old female hybrid mice, (C57BL x

CBA)F₁ (CC-1; milk-agent-free) and (CBA x C57BL)F₁ (CC-2; milk-agent-positive). A significant difference was seen in transplantability for the CC-1 and CC-2 strains; values were 17/38 (44.7%) and 49/68 (72%), resp. None of the CC-1 mice developed mammary adenocarcinoma of the grafts or host glands, as compared to 13/49 (26.5%) grafts of CC-2 mice. A similar value was determined for the development of mammary adenocarcinoma of the glands of host CC-2 mice. The CC-1 mice lived longest, with a moderate number of litters. Of the CC-2 mice, those with no mammary cancer lived the shortest time and had the fewest litters, whereas those with cancer lived longer and had the most litters. The grafts and mammary gland tissue were indistinguishable in hormone response, function, morphology and histology. It is concluded that CBA milk agent is a weak carcinogen and that the adipose tissue may be responsible for regeneration of mammary tissue and propagation of milk agent.

70-1998 SOME ASPECTS OF THE MORPHOLOGY OF THE BITTNER VIRUS. (E.) Clarke, J. K. (Vet. Res. Labs., Belfast, Ireland) and J. T. Attridge. J. Nat. Cancer Inst. 44(4):755-762, 1970.

Bittner virus morphology was examined using negatively stained, fixed (allowing better preservation of original structure and demonstration of internal components) and unfixed tumor fragments from female C3H mice with spontaneous mammary tumors. Examination showed many envelopes with rings on their surfaces sometimes appearing as a part of a more extensive reticulum. When this reticulum was detached from the virus envelope, its fine structure was seen to be composed mainly of hexagons (16.5 mμ between 2 parallel faces; max. diameter, 19.0 mμ; side length, 9.5 mμ). Virus projections were nonrandomly attached to this reticulum in a pattern corresponding to the mathematical measurement of the hexagons (a projection at each corner and center of each hexagon).

70-1999 DIRECT CELL TO CELL TRANSFER OF BITTNER VIRUS. (E.) Gay, F. W. (Queen's U. Belfast, Ireland), J. K. Clarke and E. Dermott. J. Gen. Virol. 7(1):75-79, 1970.

Electron microscopic examination of pieces of spontaneous mammary tumor from C3H mice revealed budding virus particles at cytoplasmic vacuoles and at the plasma membrane, some of which were undergoing pinocytosis by the adjacent cell even before completion of the budding process. These pinocytotic vesicles had membranes thicker and denser than the normal plasma membrane. An elongated internal component, extending from the tip to the base of the bud and which could release normal 'Immature B' particles at the expanded end, was found only where the plasma membranes of adjacent cells were apposite.

1-2000 VIRUS PARTICLES IN RAT MAMMARY TUMORS OF VARYING ORIGIN. (E.) Chopra, H. (Pfizer Co. Inc., Maywood, N. J.) and D. J. Taylor. J. Nat. Cancer Inst. 44(5):1141-1147, 1970.

Electron microscopic examination for virus particles was performed on mammary tumor tissue from various strains of rats receiving 7,12-methylbenzanthracene (DMBA), methylcholanthrene (MCA) or diethylstilbestrol-cholesterol pellets, from rats with spontaneous tumor development. Results showed frequent virus particles in the DMBA-induced and transplanted mammary tumors in Fischer rats, however no such viruses were identified in the primary DMBA-induced tumor. MCA-d pellet-induced tumors in Fischer and A x C rats, resp., revealed only extracellular particles resembling the mature C-type virus. Tumor tissue and organ cultures of the MT/Wg tumor contained a few virus-like particles but the reticulomatotropic (MtT/W5) tumor and its variant MtT/W5/OM, which metastasized to the ovary showed an enormous amount of C-type viral structures. It is suggested that the etiologic significance of the C-type virus associated with breast cancer in rats be investigated.

2-2001 ELECTRON MICROSCOPY OF THE NUCLEIC ACID OF MOUSE MAMMARY TUMOR VIRUS. (E.) Sarkar, N. H. (Inst. Med. Res., Camden, N. J.) and D. H. Moore. J. Virol. 5(2):230-236, 1970.

Mammary tumor virus (MTV) from the milk of RIII mice was purified by Ficoll density gradient centrifugation. The RNA was extracted with phenol and examined by electron microscopy. A histogram of the length distribution of 194 molecules showed distribution with a prominent peak between 1.1 and 1.3 μ m (modal length; 1.2 μ m). Another peak appeared at 2.4 μ m. Since the max. RNA molecule length was observed to be 3.6 μ m, the overall modal length (1.2 μ m) of the distribution is not likely to represent the length of an intact molecule; thus, it is probable that the length of an intact MTV-RNA molecule is 3.6 μ m.

3-2002 ENHANCEMENT BY ESTROGENS OF ADENOVIRUS OR SPONTANEOUS TRANSFORMATION OF HAMSTER CELL CULTURES. (E.) Fong, C. K. Y. (Putnam Mem. Hosp. Inst. Med. Res., Bennington, Vt.) and N. Ledinko. Cancer Res. 30(3):889-892, 1970.

When added to hamster cell cultures infected with human adenovirus Type 12, small amounts (1-50 μ g/ml) of estrogens (Premarin, containing 1-65% sodium estrone sulfate, 20-35% sodium estradiol sulfate, 2-5% α -estradiol and 15-20% dihydroequilin) produced a significant increase in rate of appearance and final numbers of viral-transformed cell foci. The formation of foci of morphologically-transformed cells in uninfected

control cultures was also stimulated by the estrogens. The transformation-enhancing effect of estrogens occurred in cultures grown in fluid and in agar, but was less in the latter. In the presence of estrogens there was increased rate of cell growth in both uninfected and infected cultures. These results indicate that estrogens stimulate growth of hamster cells *in vitro* and enhance cell transformation induced by adenovirus, as well as that which occurs spontaneously. The estrogens may act directly as carcinogens to cells, because spontaneous cell transformation was enhanced by them. It is also suggested that the enhancing effect of estrogens could be due to an increase in mitotic activity of cells altered by the virus.

70-2003 IDENTIFICATION OF A SOLUBLE TRANSPLANTATION ANTIGEN FROM THE MEMBRANE FRACTION OF ADENOVIRUS TUMOUR CELLS. (E.) Hollinshead, A. (George Washington U. Sch. Med., Washington, D. C.) and T. C. Alford. J. Gen. Virol. 5(3):411-418, 1969.

Female, 3-4-week-old Syrian golden hamsters were protected from tumor induction by adenovirus Type 12-induced tumor cells (1×10^5 cells, s.c.) after pretreatment with soluble tumor specific transplantation antigen (i.p.) from adenovirus Type 12-infected cells or induced hamster tumors. Hamsters given soluble antigen from Type 3 adenovirus-infected cells were protected after cross challenge by adenovirus Type 7 tumor cells, but were given no protection from SV40 tumor cells. The membrane fraction and the soluble antigen supernatant fluid from this fraction, as well as the tumor specific transplantation antigen fraction, protected against tumor formation more effectively than the crude tumor homogenate from which they were derived.

70-2004 RELATIONSHIP BETWEEN INDUCTION OF THYMIDINE KINASE AND POTENTIATION OF GROWTH OF H-1 VIRUS BY HUMAN ADENOVIRUS 12. (E.) Ledinko, N. (Putnam Mem. Hosp. Inst. Med. Res., Bennington, Vt.) and H. Toolan. J. Gen. Virol. 7(3):263-266, 1970.

Thymidine kinase activity of adenovirus 12-infected human embryo lung (HEL) cells was 7-8-fold higher than in noninfected cells, but this increase was reduced 50-60% after mixed infection with H-1 parvovirus. This decrease was thought to be due to H-1 growth as enzyme activity was not changed in cultures infected with H-1 alone and no dissociable inhibitors were detected in extracts from adenovirus- or H-1-infected cells. However, in HEL cells infected with adenovirus since formation of H-1 virus was almost complete by the time any increase in enzyme was detected.

70-2005 STUDY OF ONCOGENIC POTENCY OF RECENTLY ISOLATED STRAINS OF ADENOVIRUS TYPE 7.

(Fr.) Huraux, J. M. (Trousseau Hosp. Virol. Lab., Paris) and F. Bricout. Ann. Inst. Pasteur (Paris) 118(5):721-733, 1970.

In newborn Syrian hamsters inoc. with various strains of human adenovirus (AV) type 7, 26/32 strains were oncogenic and the other 6 strains were possibly so, although the number of animals was too small for significant results. Transplantation of virus-induced tumors did not produce anti-hemagglutination antibodies in the hosts. Partial crossing between the T antigens of AV types 7 and 12 was confirmed by immunofluorescence studies.

70-2006 TUMORS INDUCED IN HAMSTERS BY A RESPIRATORY-ASSOCIATED CANINE ADENOVIRUS (A26/61). (E.) Dulac, G. C. (Purdue U. Sch. Vet. Sci. Med., Lafayette, Ind.), L. J. Swango and T. Burnstein. Canad. J. Microbiol. 16(5):391-394, 1970.

Newborn, random-bred golden Syrian hamsters were inoc. with respiratory-associated (RA) canine adenovirus (Toronto A26/61 strain; 0.05 ml, s.c. or intracranially). In 6-9 mo. s.c. tumors (no metastases) developed in 4/27 animals inoc. with RA virus. Intracranial admin. of virus induced no tumors of the brain. Serial transplantation of RA-induced tumor cells in 4-7-day-old hamsters and of tissue culture-adapted tumors in weanling hamsters induced neoplasms by day 14 in those with s.c. implants and by days 15-20 in hamsters with intracranial implants. Results are comparable to those for infectious canine hepatitis virus; the 2 viruses share common T antigens, but show antigenic differences.

70-2007 MECHANISM OF MASKING OF SHOPE PAPILLOMA VIRUS IN TRANSPLANTABLE INTRAMUSCULAR TUMORS OF RABBITS. (Rus.) Nadareishvili, A. E. (Inst. Exp. Path. Ther., Sukhumi, USSR) and M. M. Tarba. Vop. Virus 14(4):407-412, 1969.

Protein fractions were obtained from extracts of Shope carcinoma and divided into 2 groups according to motility of serum γ - and β -globulins or serum albumins and α -globulins. The ability of these 2 fractions to neutralize Shope papilloma virus was studied in 40 rabbits with fractions applied to the skin (0.2 ml to 2 x 2 cm areas x 5 mo.). Complete, partial or no neutralization by the serum γ - and β -globulins occurred in 16/26, 9/26 and 1/26 rabbits, resp. For 14/14 rabbits treated with serum albumins and α -globulins, no neutralization occurred. It is suggested that non-protein components migrate with protein fractions to neutralize virus activity in carcinoma.

70-2008 CHEMICAL STUDIES ON POLYOMA AND SHOPE PAPILLOMA VIRUSES. (E.) Kass, S. J. (Weizmann Inst. Sci., Rehovot, Israel). J. Virol. 5(3):381-387, 1970.

Shope papilloma virus and polyoma virus were purified, assayed and studied by disc electrophoresis, and an essentially single polypeptide component was determined for the protein content of both. A small minor peptide was also found by sedimentation studies. Further detailed analysis showed that the polyoma virion had a molecular wt. of 22×10^6 and was comprised of 410 repeating peptide subunits.

70-2009 CHARACTERIZATION OF A TEMPERATURE-SENSITIVE MUTANT OF POLYOMA VIRUS. (E.) Fried, M. (Imperial Cancer Res. Fund, London). Virology 40(3):605-617, 1970.

Incubation of mouse embryo cells, infected with a temperature-sensitive mutant of polyoma virus (TS-a), at the nonpermissive temperature (38.5°C), inhibited production of progeny virus. Production of progeny virus increased almost to the level of that induced by the parental strain as the input multiplicities increased from 0.1-100 PFU/cell. There was no significant difference in the heat denaturation of the capsid protein or extracted DNA compared to the parental virus, nor was the temperature-sensitive step due to alterations in adsorption, release or uncoating; however, production of infectious DNA in TS-a-infected cells was decreased. Shifting to nonpermissive temperatures at various times during the growth cycle in order to determine when the temperature sensitive step occurred showed that the virus yield started to become resistant to the shift 15-23 hours after infection, and was completely resistant after 87 hours when only 40% of the final virus yield was completed.

70-2010 INDUCTION OF VIRUS SYNTHESIS IN POLYOMA TRANSFORMED CELLS BY ULTRA-VIOLET LIGHT AND MITOMYCIN C. (E.) Fogel, M. (Weizmann Inst. Sci., Rehovot, Israel) and L. Sachs. Virology 40(1):174-177, 1970.

Clones of a polyoma virus-transformed cell line, some of which spontaneously synthesized virus, were exposed to various doses of UV light or mitomycin C (MC). A sharp increase in virus synthesis was observed 2 days after UV irradiation, was dose-dependent and reached a max. of 200-fold. The increase was due to an increased number of virus-synthesizing cells. Treatment of the clones with MC (0.012 - $0.3 \mu\text{g/ml}$) resulted in a max. induction after 2 days of up to 3000-fold and was also dose-dependent. Different clones showed up to a 50-fold difference in percentage of cells with viral antigen and up to a 200-fold difference in virus yield. All clones with and 50% of clones without spontaneous induction were inducible by MC, and a conversion of clones from MC-inducible to MC-noninducible form was observed. Inhibition of cell multiplication was associated with virus synthesis.

-2011 THE FORMATION OF VARIANTS WITH A REVERSION OF PROPERTIES OF TRANSFORMED CELLS. IV. LOSS OF DETECTABLE POLYOMA TRANS-ANTIGATION ANTIGEN. (E.) Rabinowitz, Z. (Weizmann Inst. Sci., Rehovot, Israel) and L. Sachs. Virology 40(2):193-198, 1970.

Parental cells, produced in polyoma virus (PV)-transformed hamster embryo cell cultures, and which were less tumorigenic than the parental cells, demonstrated a complete loss of PV trans-antigation antigen when no immunity against the variants was induced after immunization of hamsters with $1-2 \times 10^6$ PFU i.p. Some trans-antigation resistance was induced by variant cells with a high tumorigenicity that were produced *in vivo*. The variants contact inhibited each other and inhibited the parental cells.

-2012 CHARACTERIZATION OF ABNORMAL DNA FORMED IN POLYOMA VIRUS-INFECTED CELLS. (E.) Himura, Y. (Tohoku U. Sch. Dent., Sendai, Japan), S. Katagiri and S. Aikawa. Virology (3):768-776, 1970.

Newly synthesized DNA in polyoma virus-infected mouse embryo cells ($1-100$ PFU/cell) was found, by velocity sedimentation analysis in neutral density gradients, to cosediment with DNA from uninfected cells, but with additional components representing forms I (20S) and II (6S) of viral DNA. There was no evidence of a double-stranded DNA of a molecular wt. lower than that of normal cellular DNA. Heterogeneous fragments observed in alkaline gradients were shown to derive from newly synthesized DNA and range from large fragments of a molecular wt. similar to that of normal cellular DNA to very small fragments. It is suggested that the DNA of infected cells is comprised of molecules which are double-stranded, but which carry single-strand breaks and appear normal when sedimented under neutral conditions. None of the pre-existing cellular DNA was converted to normal DNA; the appearance of abnormal cellular DNA was related temporarily to the onset of viral DNA synthesis.

-2013 IMMUNOCHEMICAL CHARACTERISTICS OF HAMSTER ANTIBODIES REACTING IN COMPLEMENT-FIXATION WITH POLYOMA VIRUS-INDUCED TUMOR ANTIGEN. (E.) Ptak, W. (Med. Acad., Krakow, Poland), M. Zembala and A. Porwit-Bober. Immunofluorescenzforsch. 139(4):340-346, 1970.

Antibodies from Syrian hamsters bearing serially-transplanted polyoma virus-induced s.c. tumors were analyzed for antibodies reacting with polyoma virus-induced complement-fixing tumor antigens by Sephadex columns, chromatography and immunoelectrophoresis. Complement-fixing activity against tumor antigens consisted of a heterogeneity of 7S immunoglobins similar to those seen in mice and guinea pigs.

70-2014 EFFECT OF ULTRAVIOLET IRRADIATION AND ACTINOMYCIN D ON POLYOMA VIRUS REPLICATION IN MOUSE EMBRYO CELL CULTURES. (E.) Bowen, J. M. (U. Texas M. D. Anderson Hosp. Tumor Inst., Houston), R. G. Hughes and L. Dmochowski. J. Virol. 3(6):570-577, 1969.

Swiss mouse embryo (ME) cell cultures were treated with UV irradiation ($60 \mu\text{watts/cm}^2 \times 15, 20$ or 45 seconds) or actinomycin D (A-D; 0.1 or $0.3 \mu\text{g/ml} \times 1$ or 6 hours) and infected with polyoma virus or encephalomyocarditis (EMC) virus. Replication of EMC virus was unaffected by max. UV dose and only slightly impaired by A-D. Polyoma virus replication decreased as UV dosage increased and as A-D conc. and exposure time increased. Polyoma T antigen synthesis was not affected by either UV or A-D admin. UV irradiation of cells during infection almost abolished DNA and RNA synthesis. DNA and RNA synthesis was impaired in cells treated with A-D or UV prior to viral infection. It is concluded that inhibitory effects on polyoma virus replication in ME cell culture occur early after infection, and that functional integrity of the ME cell genome is required for polyoma virus replication, but not for EMC.

70-2015 IMMUNOLOGIC TOLERANCE AND ADOPTIVELY TRANSFERRED IMMUNITY IN POLYOMA VIRUS TUMOR REPRESSION. (E.) Law, L. W. (NCI, Bethesda, Md.). Life Sci. 8, Pt. 2(20):1079-1082, 1969.

C3H/BI mice, susceptible to the oncogenic effects of polyoma virus, were divided into 4 groups: group 1 (21 mice) received 2×10^6 FFU polyoma virus s.c. at 8 days of age; group 2 (21 mice) was inj. i.v. at birth with 10^7 splenic lymphoid cells from C3H/Lw (resistant) mice, then received virus at 8 days; group 3 (14 mice) was inj. with virus as above, then received C3H/Lw lymphoid cells 30 days later; and group 4 (31 mice) was inj. with adult C3H/Lw cells at birth and sensitized C3H/Lw lymphoid cells (from adult mice inoc. with polyoma virus and then challenged with a virus-specific transplantation antigen) 30 days after virus inoc. The latent period of tumor formation was 3.3, 5.2, 5.1 and 8.0 mo., resp., and the number of mice with tumors was 81%, 76%, 65% and 16%, resp. Thus, adoptively transferred resistance was accomplished between allogeneic strains.

70-2016 MORPHOLOGICAL DIFFERENCES OF EXPERIMENTAL TUMORS IN HAMSTERS DUE TO POLYOMA VIRUS. (It.) Puccini, C. (Via Fossato di Mortara 64, Ferrara, Italy) and B. Montalto. Boll. Ist. Sieroter. Milan. 48(4):324-342, 1968.

Tumors were induced in newborn hamsters inoc. with 2 polyoma viruses (CET and RTT; s.c.); the tumors were mostly multiple, of connective or vascular tissue origin, and located in such

organs as the liver (72), heart (67), lungs (59), mediastinum (46), kidneys (31), at inj. site (11), and brain and small intestine (1 each). Differentiation of tumors was according to localization and tissue involved, with fibrosarcomas, fibromas and fibromyxomas, spindle and round cell sarcomas, cystic angiomas and other sarcomas observed.

70-2017 MORPHOGENESIS OF EXPERIMENTAL TUMORS INDUCED BY POLYOMA VIRUS IN NEWBORN HAMSTERS. (It.) Puccini, C. (Via Fossato di Mortara 64, Ferrara, Italy) and B. Montalto. Boll. Ist. Sieroter. Milan 48(4):343-357, 1969.

The morphogenesis of tumors induced by inoc. of 2 polyoma viruses (CET and RTT) in newborn hamsters is discussed. Heart and kidney sarcomas developed upon stimulation of undifferentiated mesenchymal cells, followed by transformation of these cells to fibroblastic form and production of intracellular substance. Simple and neoplastic cystic tumors of the lungs and liver arose from modifications of vascular endothelium and perivascular mesenchyme. Solid angioblastic (or mesenchymal) tumors of the liver and kidneys had growth characteristics similar to connective tissue tumors. The multipotential action of polyoma viruses on different cells is indicated by the polymorphism of tumor cells.

70-2018 HISTONE SYNTHESIS IN POLYOMA- AND SV40-INFECTED CELLS. (E.) Winocour, E. (Weizmann Inst. Sci., Rehovot, Israel) and E. Robbins. Virology 40(2):307-315, 1970.

Histone synthesis in various cell cultures was measured by acrylamide gel electrophoresis of ^3H -tryptophan- and ^{14}C -lysine-labeled acid-soluble nuclear proteins. A stimulation of histone synthesis over that in uninfected cells was observed in contact-inhibited or X-irradiated (5000 rads) 3T3 mouse cells infected with SV40, and in polyoma virus-infected primary mouse kidney cells and hamster BHK21 cells. Mitotic activity was also observed in the X-irradiated SV40-infected 3T3 cells.

70-2019 COLLAGEN-GALACTOSYL TRANSFERASE: SUBCELLULAR LOCALIZATION AND DISTRIBUTION IN FIBROBLASTS TRANSFORMED BY ONCOGENIC VIRUSES. (E.) Bosmann, H. B. (U. Rochester Med. Sch., N. Y.). Life Sci. 8, Pt. 2(14):737-746, 1969.

About 70% of collagen:galactosyl transferase (C:G-TA) in HeLa cell fractions, when a specific acceptor was added, was found in the 4000 x g supernatant and 30% in the 4000 x g pellet. Almost 90% of the activity in the supernatant fraction was contained in the plasma membrane fraction. Endogenous activity (at pH 6), found in the smooth internal membranes, was due to the activity of glycoprotein:galactosyl transferase,

while endogenous activity found in plasma membranes was due to C:G-TA. In polyoma (PY)- and simian virus (SV)-transformed mouse fibroblast lines (PY-3T3, SV-3T3, SV-PY-3T3), although endogenous activity was elevated, the C:G-TA when an acceptor was added was only half that of nontransformed lines (3T3-Va and 3T6). No elevation in β -galactosidase activity was found at pH 6.0 in the transformed cells.

70-2020 VARIATIONS IN THE NUMBER OF NUCLEOLI IN NORMAL AND IN SV40 VIRUS INFECTED HUMAN CELL CULTURES. (E.) Sapatino, V. (St. S. Nicolau Inst. Inframicrobiol., Bucharest, Rumania), I. Aderca and M. Iftimovici. Rev. Roum. Inframicrobiol. 6(3):203-210, 1969.

Human embryo cell cultures (EU) were inoc. with SV40 (0-2 ml; 10^7 TCID₅₀/ml). In cell lines given 2 ml of virus (EU₁), the percentage of nuclei with a single nucleolus was 45% at passage 4 (16 days) and fell to 1% by passage 28 (123 days), while those nuclei with 2 or more nucleoli increased with time up to 97% at passage 43 (162 days). A similar trend (the mean number of nucleoli/nucleus increasing) was seen in cells inoc. with 1 ml of virus (EU₂). In cells given no virus the opposite trend was observed. Cellular transformation of the epithelial type began in EU₁ at passage 4 and in EU₂ at passage 7; the number of transformed cells and rate of proliferation increased with time.

70-2021 SIMIAN VIRUS 40-INDUCED T AND TUMOR ANTIGENS. (E.) Potter, C. W. (U. Sheffield, England), B. C. McLaughlin and J. S. Oxford. J. Virol. 4(5):574-579, 1969.

Hamsters were inoc. with SV40-induced tumor cells (10^5 cells, s.c.) and tumors transplanted to 3-day-old hamsters. Rate-zonal centrifugation of tumor extracts from these animals showed 3 molecular forms of antigen, with the major portion having a molecular weight of 65,000-75,000. These results were further substantiated by sucrose gradient analysis. In studies with T antigen induced by SV40 in BSC-1 cells, 3 similar peaks were found, but quantitative differences between tumor and T antigen species were seen.

70-2022 TRANSPLANTED CELL LINES TRANSFORMED BY SV40 VIRUS IN TISSUE CULTURE. (Rus.) Sarycheva, O. F. (L. A. Tarasevich State Control Inst. Med. Biol. Preps., Moscow), N. N. Dodonova, N. N. Vasil'eva, A. F. Bykovskii and A. D. Al'tshtein. Vop. Onkol. 15(12):69-75, 1969.

Transplanted cell lines (CL; total 43) of embryonic or renal tissue from Syrian hamsters, mice (strains C57BL, CC57Br, C3Hf) and Wistar rats were transformed by SV40. The morphology

transformed cells was dependent on the morphology of the primary target cell. The rat embryonic CL had fibroblast-like cells with cleoli and nuclei of various forms and sizes. Mouse embryonic CL showed multilayered growth of polygonal and spindle-shaped cells. Hamster embryonic CL showed the most uniform fibroblast-like structure. Hamster renal CL had markedly aligned epithelial-like cells with polymorphic clei and fibroblast-like cells in irregular layers. Mouse renal CL were similar. All had significant variability in chromosome number, and all CL, independent of structure or origin, contained T antigen of SV40.

-2023 DETECTION OF SV40-INDUCED T ANTIGEN IN PERIPHERAL LEUKOCYTES OF TUMOR-BEARING MICE. (E.) Jamison, R. M. (U. Colorado Med. Ctr., Denver). Cancer Res. 30(5):1541-1543, 1970.

Direct and indirect fluorescent antibody staining methods performed on WBC of hamsters with transplanted fibrosarcomas (induced by SV40 papovavirus) detected T antigen; whereas the SV40 renal antigen was not found by either method. The indirect method was more sensitive for finding positive cells. WBC of hamsters with polyoma virus-induced tumors did not react with any test sera.

-2024 ANALYSIS OF SV40-INDUCED TRANSFORMATION OF HAMSTER KIDNEY TISSUE IN VITRO. VI. CHARACTERISTICS OF MITOMYCIN C INDUCTION. (E.) Hynes, W. H. (Harvard Med. Sch., Boston, Mass.) and P. H. Black. Virology 39(4):625-634, 1969.

In a series of experiments with cell lines of mammalian origin (baby hamster kidney, mouse embryo and kidney, human buccal mucosa and embryonic green monkey kidney), administration of mitomycin C (MC; 0.1-50 µg/ml x 8 or 20 hours) to SV40-transformed hamster kidney cell lines (HK-21, T8-AP1) induced infectious SV40 at MC concentrations from 0.3-5 µg/ml, with no direct relationship between MC concentration and virus yield. Passage *in vivo* increased virus yield after MC induction. Treatment of T8-AP1 cell cultures with MC (1.0 µg/ml x 8 hours) and cytosine arabinoside (CA; 5 µg/ml for various time periods) indicated that a synthesis is necessary from 24-36 hours after beginning MC treatment in order that virus be produced. A homologous interferon preparation, assay studies with T8-AP1 cells, inhibited induction of transformed cells. Similar experiments with SV40-transformed cell lines of other species and other DNA-type virus-transformed cells were unsuccessful. A similarity between SV40-transformed cells and bacterial lysogeny, and their possible relationship to mammalian plasmids, is suggested.

-2025 RESISTANCE OF TRANSFORMED MONKEY KIDNEY CELLS TO SUPERINFECTION WITH SV40.

(Ger.) Sauer, G. (German Cancer Res. Ctr. Inst. Virus Res., Heidelberg) and E. Hahn. Zbl. Bakt. [Orig.] 212(2-4):399, 1970.

Transformation of cells was only obtained when cells underwent mitotic cell division after infection with SV40. The lower the cell density, the greater was the number of surviving colonies of transformed cells. These transformed cells, with no virus envelope protein, did not produce infectious virus but contained tumor antigen and were resistant to superinfection with SV40. After superinfection, the virus was adsorbed by these cells but did not multiply. The virus lost its infectivity within 2-3 days, but small amounts of infectious SV40 DNA were still detected (no details). The inability of SV40 DNA to induce productive infection could be due to a blocking of the "uncoating" process or to an absence of transcription of all viral gene functions.

70-2026 TRANSFORMATION OF BSC1 CELLS FOLLOWING CHRONIC INFECTION WITH SV40. (E.) Margalith, M. (Hebrew U.-Hadassah Med. Sch., Jerusalem), R. Volk-Fuchs and N. Goldblum. J. Gen. Virol. 5(3):321-327, 1969.

The majority of BSC1 cells, infected with SV40 (0.1-100 PFU/cell) demonstrated a cytopathic effect after 3 weeks, but in cultures infected with multiplicities of 10 and 100, a small number of cells were unaffected and developed into colonies (BSC/SV40). Studies of the BSC/SV40 cells during passages 7-44 showed that the number of cells able to produce infectious virus decreased from 100% to 0.2%, while the cells stained for viral antigen decreased from 4.2% to 0.01% and the percentage with tumor antigen increased from 4% to 100%. Antiserum to virus, actinomycin D and cytosine arabinoside completely inhibited synthesis of both virus and tumor antigens in the carrier cultures, but affected only the virus antigen in transformed cells. The transformed cells were susceptible to superinfection with herpes simplex, poliovirus type 1, and vaccinia, but not with SV40. Cell cloning yielded 2 virus-free clones.

70-2027 INDUCTION OF SIMIAN VIRUS 40 ANTIGEN IN BSC1 TRANSFORMED CELLS. (E.) Margalith, M. (Hebrew U. Hadassah Med. Sch., Jerusalem), E. Margalith, T. Nasalski and N. Goldblum. J. Virol. 5(3):305-308, 1970.

A culture of SV40-transformed BSC1 monkey kidney cells produced SV40 viral antigen when heated to 45° C for 30 min.; infectious virus, however, was not detected. Viral antigen was seen in 3.8% of the cells after 72 hours, and this was increased to 11% upon depletion of arginine from the medium. Cytosine arabinoside, on the other hand, completely inhibited production of viral antigen. Cell fusion with the BSC1-transformed cells and rabbit kidney cell line MA-111 showed

infectious SV40 virus, as did treatment with mitomycin C.

70-2028 TRANSFORMATION OF MOUSE 3T3 CELLS BY T ANTIGEN-FORMING DEFECTIVE SV40 VIRIONS (T PARTICLES). (E.) Uchida, S. (Nat. Inst. Health, Shinagawa-ku, Tokyo) and S. Watanabe. Virology 39(4):721-728, 1969.

Mouse 3T3 cells infected with defective deletion mutants of SV40 or plaque-formers had a transformation frequency directly proportional to the virus dose up to 3×10^8 T antigen-forming units. Cells from colonies showed loss of contact inhibition, were positive for T antigen, were virus-free, but were negative for V antigen and only had weak anti-T fluorescence. These cells were fused with African green monkey kidney cells and the resulting heterokaryons produced V antigen only when derived from the plaque-formers. The V antigen-producing heterokaryons demonstrated an increase in anti-T fluorescence, possibly due to viral replication. It is suggested that the strongly fluorescent T-antigen in the nucleus of the heterokaryons from the defective virus was due to replication of the defective T particle genome. Nuclear alterations in the heterokaryons are described.

70-2029 TRANSFER RNA FROM TUMOR TISSUE. (E.) Hall, R. H. (McMaster U., Hamilton, Ontario, Canada). J. Cell Physiol. 74(2, Pt. 2): 155, 1969.

The uptake and incorporation of methyl groups after incubation with ^{14}C -methylmethionine were compared in enzyme preparations from SV40-induced hamster tumors and normal tissues, in Burkitt lymphoma cells and in normal human lymphocytes. The data suggest a qualitative and quantitative difference in methylating pattern between normal and tumor cells.

70-2030 TRANSFER RNA METHYLASE ACTIVITIES OF SV40-TRANSFORMED CELLS AND CELLS INFECTED WITH ANIMAL VIRUSES. (E.) Kit, S. (Baylor Coll. Med., Houston, Tex.), K. Nakajima and D. R. Dubbs. Cancer Res. 30(2):528-534, 1970.

No significant difference was observed in the transfer RNA (tRNA)-methylating enzyme activity (measured with limiting amounts of enzyme) or capacity (measured with limiting amounts of tRNA) of African green monkey kidney cells (CV-1) and mouse kidney cell cultures after infection with SV40, herpes simplex or vaccinia. Thymidine kinase activity, however, was enhanced by all 3 viruses. In mouse kidney cells transformed by SV40, tRNA-methylase activity and capacity was increased 2-4-fold, increasing with exponential growth of the cells and declining in the stationary growth phase. As these fluctuations were markedly less than those of thymidine kinase

activity, they probably do not account for the high tRNA methylase levels in transformed cells.

70-2031 CAPSID PROTEINS OF SIMIAN VIRUS 40. (E.) Girard, M. (Sci. Res. Inst. Cancer, Villejuif, France), L. Marty and F. Suarez. Biochem. Biophys. Res. Commun. 40(1): 97-102, 1970.

Cultures of CV₁ cells were infected with SV40 virus, labeled on days 5-7 with ^{14}C -labeled amino acids, and the virus was purified. The virions were further disrupted by sodium dodecyl sulfate, 1% β -mercaptoethanol and heat. Electrophoresis showed 6 polypeptide chains (capsid proteins) in the purified SV40 virions, including 3 major and 3 minor components. The molecular weights determined for the proteins were 45,000, 35,000, 35,000, 18,000, 14,000 and 10,000.

70-2032 ENCAPSIDATION OF FREE HOST DNA BY SIMIAN VIRUS 40: A SIMIAN VIRUS 40 PSEUDOVIRUS. (E.) Trilling, D. M. (New York State Dept. Health, Albany) and D. Axelrod. Science 168(3928):268-271, 1970.

Encapsulation of host DNA was produced by purified small plaque SV40 cultured on green monkey cell lines. Density gradient studies revealed 2 bands, with a noncircular form free of viral DNA, of lower molecular wt., in the upper band with host DNA. Hybridization studies further separated the character of host and viral DNA. The encapsidated DNA is linear and smaller than SV40 DNA. Such "pseudovirions" have sufficient host DNA for protein coding, and indicate a mechanism for gene transfer between host cells.

70-2033 INACTIVATING AND MUTAGENIC EFFECTS OF NITROSOGUANIDINE ON SIMIAN VIRUS 40. (E.) Tegtmeyer, P. (Case Western Reserve U., Cleveland, Ohio), C. Dohan, Jr. and C. Reznikoff. Proc. Nat. Acad. Sci. USA 66(3):745-752, 1970.

Admin. of N-methyl-N'-nitro-N-nitrosoguanidine (NG; 100-5000 $\mu\text{g}/\text{ml}$ \times 3 hours) to extracellular SV40 resulted in 90% loss of infectivity for the 500 μg conc. Partially NG-inactivated virions, however, had no mutants. Continuous exposure of SV40-infected cells to NG (0.625-40 $\mu\text{g}/\text{ml}$) gave a virus yield close to that of controls or a yield equal to residual virus inoculum, with marked toxic effect, for the low to high conc. range, resp. Inhibition was partial for intermediate conc. (2.5-10 $\mu\text{g}/\text{ml}$). NG treatment of SV40-infected cells resulted in 6 plaque mutants and 6 temperature-resistant mutants. It is concluded that the virus protein coat does not block NG inactivation of SV40, but that loss of infectivity does not necessarily represent successful mutagenesis of SV40 by NG.

2034 PARTIAL PURIFICATION OF THE EPSTEIN-BARR VIRUS AND SOME PROPERTIES OF ITS A. (E.) Schulte-Holthausen, H. (U. Wurzburg Inst. Virol., Germany) and H. zur Hausen. Virology 40(3):776-779, 1970.

procedure using sucrose gradient sedimentation which selectively concentrates enveloped particles of Epstein-Barr virus (not penetrable by phosphotungstic acid) from the P3HR-1 clone of Burkitt lymphoma cells is described. Equilibrium centrifugation in CsCl indicated a guanine + cytosine content of 59%.

2035 CYTOCHEMICAL STUDY ON THE NATURE OF NUCLEIC ACIDS IN EPSTEIN-BARR VIRUS (EBV). (E.) Chai, L. S. (Roswell Park Mem. Inst., Buffalo, N. Y.), J. S. Horoszewicz and T. Grace, Jr. J. Surg. Oncol. 1(3):273-281, 1969.

He 64-10 cells infected with Epstein-Barr virus (EBV) were embedded in glycol-methacrylate and exposed to 0.2% wt./vol. DNase or RNase and the nucleic acids present in the nucleoids examined. An analysis of 100 extracellular virus particles, DNase treatment revealed dense, partial or no nucleoids in 20%, 43% and 37%, resp., while RNase treatment resulted in dense, partial or no nucleoids in 96%, 0% and 4%, resp. These results indicate that EBV contains DNA since the nucleoid regions of the virus particles are susceptible to digestion with DNase but not with RNase or trypsin (control). This finding is similar to that found with herpes viruses.

2036 MULTIPLICATION OF VIRUSES IN BURKITT LYMPHOMA CELLS. (E.) Chung, M. (U. Michigan Sch. Med., Ann Arbor), B. I. Ma and H. Murphy. J. Nat. Cancer Inst. 44(6):1231-1239, 1970.

A series of viruses were grown in cultures of P3J Burkitt lymphoma cells (sublines of the Epstein-Barr (EB) virus, P3J-EB⁺ (virus rich) and P3J-EB⁻ (virus poor)) to determine most effective multiplicity of infection (MOI). The highly cytopathic vesicular stomatitis virus had an MOI of 0.1, with 95% of the cells of both cell lines dead by day 4. For the mumps virus with an MOI of 0.005, 50% of the cells were infected by 4-6 days, especially with the P3J-EB⁺ line. Parainfluenza virus types 1, 2 and 3 (PI-1, -2 and -3) were tested and gave varied results. PI-3 was cytopathic to 85% of the cells, as opposed to only 20% for the others, but PI-1 growth increased 16- to 32-fold. For measles virus, the MOI was 0.001. Giant cell formation by aggregation of infected Burkitt cells, found as early as 9 hours after measles virus infection, was studied to determine the mechanism of their growth. It was not determined that an increase in EB virus particles in superinfected cells had occurred.

70-2037 OCCURRENCE OF ANTIBODIES AGAINST THE BURKITT VIRUS (EPSTEIN-BARR VIRUS, EBV). (Ger.) Gallmeier, W. M. (Ruhr U. Essen Tumor Res. Clin., Germany), C. Hertenstein, C. G. Schmidt and E. Titzschkau. Deutsch. Med. Wschr. 95(24):1297-1301, 1970.

Indirect immunofluorescence and immunoprecipitation (Ouchterlony) tests were performed on sera from 4 normal persons (Burkitt lymphoma contacts), 3 pts. with infectious mononucleosis (IM) and 33 tumor pts. including 1 case of Burkitt's lymphoma, 8 lymphosarcomas, carcinomas of the larynx (12), tonsils (3); tongue, cheek, lips and bronchi (1 each) and ovaries (4) and 1 reticulum cell sarcoma. Burkitt's lymphoma cell lines were used as antigens. The Ouchterlony test was positive for 7/38 sera (the Burkitt's lymphoma, 2 lymphosarcomas, 3 nose-throat carcinomas and 1 normal), while the indirect immunofluorescence test was positive for 35/38 sera. For the latter test, elevated titers (greater than 1:80) were seen in 1/3 with IM, 4/7 with lymphosarcoma, 3/17 with nose-throat carcinoma and for Burkitt's lymphoma (1:640). No definite correlation was found between the 2 tests, but all sera positive by the Ouchterlony method showed titers of 1:80-1:160 in comparison to the immunofluorescence test. It is concluded that Epstein-Barr virus occurs also in Germany.

70-2038 SEROEPIDEMIOLOGICAL STUDIES ON NASOPHARYNGEAL CARCINOMA BY FLUORESCENT ANTIBODY TECHNIQUES WITH CULTURED BURKITT LYMPHOMA CELLS. (E.) Kawamura, A., Jr. (U. Tokyo Inst. Med. Sci., Minato-ku), M. Takada, A. Gotoh, K. Hamajima, T. Sanpe, M. Murata, Y. Ito, T. Takahashi, T. Yoshida, T. Hirayama, S.-M. Tu, C.-H. Liu, C.-S. Yang and C.-H. Wang. Gann 61(1):55-71, 1970.

After standardization of fluorescent antibody test methods, an anti-Epstein-Barr (EB) virus titer greater than 1:640 was found in sera of 85.7% of Burkitt lymphoma (BL) pts., 77.1% of Chinese pts. with nasopharyngeal carcinoma (NPC) in Taiwan and 63.56% of Japanese pts. with NPC, compared with 15% of pts. with lymphomas, leukemias and other neoplastic diseases and 5-15% in normal subjects. Sera from pts. with infectious mononucleosis had lower titers than those with NPC and BL. The presence of a similar antibody, with identical or similar reactivity against EB-virus, in the sera of both NPC and BL pts. is suggested.

70-2039 ANTIBODY PATTERNS IN DIFFERENT HUMAN SERA AGAINST INTRACELLULAR AND MEMBRANE-ANTIGEN COMPLEXES ASSOCIATED WITH EPSTEIN-BARR VIRUS. (E.) Svedmyr, A. (Stockholm City Cent. Biol. Lab.), A. Demissie, G. Klein and P. Clifford. J. Nat. Cancer Inst. 44(3):595-610, 1970.

Sera from African pts. with Burkitt's lymphoma (BL; 3), nasopharyngeal carcinoma (NPC; 3), 1 healthy brother of a BL pt. and Swedish or American donors with known anti-Epstein-Barr virus (EBV) titers (5, including 2 with a known history of infectious mononucleosis) and their fluorescein-conjugated immunoglobulins were compared for anti-EBV and EBV-associated membrane-antigen reactivity by cross-blocking tests in direct immunofluorescence on fixed and viable cells, resp. Some sera had complete cross-reactivity by blocking, but some asymmetries were found in both membrane and anti-EBV tests, with blocking obtained in only 1 direction and not reciprocally. It was assumed that both the intracellular and membrane-antigen systems consisted of more than 1 antigenic component; thus, some EBV-positive sera would have antibodies against a larger number of components than others. For some combinations of serum, cross-blocking patterns obtained in the anti-EBV test correlated well with corresponding blocking patterns in the membrane test, but some other serum combinations gave discordant results in the 2 tests. The most complete serum, containing the largest number of anti-EBV and membrane-reactive antibody components, was derived from a 38-yr.-old man with NPC, while that with the least antibody components was from the 18-yr.-old healthy brother of a pt. with BL. The possibility that broadness of immunization is related to case history, especially to persistence of a tumor mass, is discussed.

70-2040 Herpesvirus saimiri. I. FURTHER CHARACTERIZATION STUDIES OF A NEW VIRUS FROM THE SQUIRREL MONKEY. (E.) Meléndez, L. V. (New England Reg. Primate Res. Ctr., Southboro, Mass.), M. D. Daniel, F. G. Garcia, C. E. O. Fraser, R. D. Hunt and N. W. King. Lab. Anim. Care 19(3):372-377, 1969.

Herpesvirus saimiri isolated from squirrel monkeys failed to produce a cytopathogenic effect (CPE) after inoc. in mouse, hamster, cat, dog, cebus monkey, Macaca cyclopis, deermouse or human embryo cell cultures. A CPE was seen, however, in kidney cultures from African green, owl and marmoset monkeys and Vero cells. The morphology of these cells is described. Acute and convalescent infectious mononucleosis sera (diluted 1:5) did not neutralize the CPE in owl monkey cells. The neutralization index of pooled sera was about 2.0 in uninoculated squirrel monkeys, and not higher than 2.5 in hyperimmunized monkeys after week 2. No antibody could be produced in rabbits. Inoc. with Herpesvirus saimiri produced no clinical symptoms in chick embryos, mice or squirrel monkeys, but induced acute malignant lymphoma in owl and marmoset monkeys.

70-2041 Herpesvirus saimiri. II. EXPERIMENTALLY INDUCED MALIGNANT LYMPHOMA IN PRIMATES. (E.) Meléndez, L. V. (New England Reg. Primate

Res. Ctr., Southboro, Mass.), R. D. Hunt, M. D. Daniel, F. G. Garcia and C. E. O. Fraser. Lab. Anim. Care 19(3):378-386, 1969.

Cotton top marmoset monkeys (6) were inoc. i.m. and by corneal scarification with 0.5 ml Herpesvirus saimiri. All animals became inactive and lethargic prior to death within 18-22 days and inocula from liver and kidney tissue, and from oral and anal swabs taken at various times postinfection, produced a cytopathogenic effect (CPE) in marmoset kidney cultures. Another group of 6 marmoset monkeys similarly inoc. with unheated, frozen virus all died within 13-28 days. A CPE was observed with inocula from tissue samples and swabs, but was mainly due to Herpesvirus hominis. The gross and histopathological appearance was described and found consistent, in both groups, with malignant lymphoma of the reticular cell type. Monkeys treated with virus heated at 56° C for 1 hour were unaffected. Similar findings were obtained in owl monkeys.

70-2042 Herpesvirus saimiri. V. FURTHER EVIDENCE TO CONSIDER THIS VIRUS AS THE ETIOLOGICAL AGENT OF A LETHAL DISEASE IN PRIMATES WHICH RESEMBLES A MALIGNANT LYMPHOMA. (E.) Meléndez, L. V. (New England Reg. Primate Res. Ctr., Southboro, Mass.), M. D. Daniel, R. D. Hunt, C. E. O. Fraser, F. G. Garcia, N. W. King and M. E. Williamson. J. Nat. Cancer Inst. 44(5):1175-1181, 1970.

A cell culture preparation from the left kidney of an owl monkey with terminal malignant lymphoma due to previous inoc. with Herpesvirus saimiri (derived from squirrel monkey kidney isolate) was inoc. into 6 owl monkeys after passage through 100 or 220 mμ filters. Two of these 6 animals showed lesions (reticulum cell infiltrate) similar to those of animals producing the culture, while 3/3 receiving the 100 mμ filtrate showed no lesion suggestive of H. saimiri. All 3 marmoset monkeys also inoc. with this culture showed lesions characteristic of H. saimiri-induced malignant lymphoma. Results support consideration of H. saimiri as the etiological agent of the experimentally induced malignant lymphoma of the reticulum cell type in nonhuman primates.

70-2043 GENITAL HERPES VIRUS FINDINGS IN RELATION TO CERVICAL NEOPLASIA. (E.) Royston, I. (Johns Hopkins U. Sch. Med., Baltimore, Md.), L. Aurelian and H. J. Davis. J. Reprod. Med. 4(4):9-13, 1970.

Antibody to genital herpes virus type 2 (HSV-2) was found in about 100% of pts. with confirmed invasive carcinoma or carcinoma in situ of the cervix. Comparison with controls or pts. with carcinomas of other sites indicates this is significant. Oral herpes virus type 1 (HSV-1)

no significant relationship to carcinoma; 1 groups were about 85% positive for HSV-1. Her venereal diseases were similarly prevalent in carcinoma pts. or control groups. Because peak age for HSV-2 infection is over 20 yr. earlier than for invasive carcinoma, it is concluded that HSV-2 is related to induction, rather than multiplication, of neoplastic cells.

70-2044 SIMILAR VIRUS-LIKE PARTICLES FOUND IN CANCERS OF THE PROSTATE AND BREAST. (E.) Tannenbaum, M. (Columbia U. Coll. Phys. Surgeons, New York, N. Y.) and J. K. Lattimer. J. Urol. 103(4):471-475, 1970.

The same type virus-like particles found directly in cancerous areas of the breast were found directly in cancerous areas, as well as in cells adjacent to cancerous areas, of the prostate. Preliminary studies have shown these particles present in 1/3 human semen specimens examined. Configuration and measurements are the same as for the Lucké tumor virus.

70-2045 INDUCTION OF RENAL TUMORS IN TRIPLOID LEOPARD FROGS. (E.) McKinnell, R. G. (Tulane U., New Orleans, La.) and K. W. Tweedell. J. Nat. Cancer Inst. 44(5):1161-1166, 1970.

Tumor fractions from a renal adenocarcinoma of a female *Rana pipiens* frog were inj. into triploid and normal larvae. By 1 mo. after metamorphosis, 12/23 (44%) triploid and 12/17 (71%) diploid frogs developed renal carcinomas. The tumors (all noninclusion-type) of the two groups did not differ histologically, but the triploid tumor volume was greater than expected. Although the frequency of tumors was less for the triploid frogs, there is no evidence that they are more resistant to tumor formation. The results support the evidence that components of tumor cell fractions can transform normal cells.

70-2046 BIOLOGIC DIFFERENTIATION OF 3 LEUKEMIAS OF SIMILAR CELL TYPE. (E.) Nielsen, A. H. (U. Kansas Sch. Med., Kansas City), H. Cogen, O. J. Mira and A. A. Werder. Fed. Proc. 28(2):750, 1969.

70-2047 SUSCEPTIBILITY TO FRIEND VIRUS LEUKEMIA DURING DEVELOPMENT OF VIRUS-INDUCED THYMIC LYMPHOMA. (E.) Rich, M. A. (Albert Einstein Med. Ctr. Res. Labs., Philadelphia), P. S. Karl and R. Clymer. Fed. Proc. 28(2):31, 1969.

70-2048 DELAYED ONSET OF COOMBS POSITIVE HEMOLYTIC ANEMIA IN LEUKEMIA VIRUS-INDUCED NEW ZEALAND BLACK MICE. (E.) Morton, J. L. (U. Oregon Med. Sch., Portland), D. Melby and B. V. Siegel. Fed. Proc. 29(2):435, 1970.

70-2049 CYTOLYTIC ACTIVITY OF ARBOVIRUSES IN MURINE LEUKEMIC LYMPHOBLASTS. (E.)

Stim, T. B. (Yale U., New Haven, Conn.) and W. G. Downs. Fed. Proc. 28(2):698, 1969.

70-2050 THEORETICAL MODELS OF SARCOMAGENESIS. (E.) Siegler, R. (New England Deaconess Hosp. Cancer Res. Inst., Boston, Mass.). Fed. Proc. 28(2):297, 1969.

70-2051 OUTBREAK OF RETICULUM CELL SARCOMA IN A SEGREGATED COLONY OF JAPANESE QUAIL. (E.) Nishimura, E. T. (U. Hawaii Med. Sch., Honolulu), G. Leslie and E. Ross. Fed. Proc. 28(2):750, 1969.

70-2052 STUDIES ON RETICULUM CELL SARCOMA IN HAMSTER. (E.) Gerber, M. (Northwestern U. Chicago Med. Sch., Ill.), S. R. Rohlfing, E. R. Brown and S. O. Schwartz. Fed. Proc. 28(2):314, 1969.

70-2053 VIRUS-INDEPENDENT IMMUNOGENICITY OF SPONTANEOUS MAMMARY CARCINOMAS OF MICE. (E.) Weiss, D. W. (Hebrew U., Jerusalem), L. Young and M. Adelberg. Fed. Proc. 29(2):573, 1970.

70-2054 AMINOACYLATION OF ONE OF THE TWO RNA COMPONENTS ISOLATED FROM AN ONCOGENIC VIRUS. (E.) Erikson, R. L. (U. Colorado Med. Sch., Denver) and E. Erikson. Fed. Proc. 28(2):846, 1969.

70-2055 SYNTHESIS AND MORPHOGENESIS OF ADENOVIRUS CAPSID PROTEINS. (E.) Velicer, L. F. (U. Pennsylvania Sch. Med., Philadelphia) and H. S. Ginsberg. Fed. Proc. 28(2):906, 1969.

70-2056 MECHANISM OF ENHANCEMENT OF ADENOVIRUS TYPE 2 BY SV40 VIRUS. (E.) Friedman, M. P. (U. Pennsylvania Sch. Med., Philadelphia), M. J. Lyons and H. S. Ginsberg. Fed. Proc. 28(2):698, 1969.

70-2057 DEGRADATION AND INTEGRATION OF ADENOVIRUS TYPE 12 DNA IN ABORTIVE INFECTION OF HAMSTER CELLS. (E.) zur Hausen, H. (Child. Hosp. Philadelphia, Pa.) and F. Sokol. Fed. Proc. 28(2):914, 1969.

70-2058 DEVELOPMENTAL RESISTANCE TO POLYOMA VIRUS ONCOGENESIS AND RUNTING IN MICE TREATED WITH ALS. (E.) Al-Falluji, M. M. (Ohio State U., Columbus), J. P. Minton and M. C. Dodd. Fed. Proc. 28(2):768, 1969.

70-2059 DENATURATION PATTERN OF THE DNA OF ADENOVIRUS TYPE 2 AS DETERMINED BY ELECTRON MICROSCOPY. (E.) Doerfler, W. (Rockefeller U., New York, N. Y.) and A. K. Kleinschmidt. Fed. Proc. 29(2):725, 1970.

70-2060 PURIFICATION AND PROPERTIES OF AN ENDONUCLEASE FROM BABY HAMSTER KIDNEY CELLS TRANSFORMED BY POLYOMA VIRUS. (E.) Koh, J. K. (U. Maryland Sch. Med., Baltimore), A. D. Waddell and H. V. Aposhian. Fed. Proc. 29(2):406, 1970.

70-2061 ATTEMPTED RESCUE OF EB VIRUS BY SUPERINFECTION WITH HERPES SIMPLEX VIRUS. (E.) Floyd, R. (Baylor U. Coll. Med., Houston, Tex.), V. Vonka, D. D. Porter and M. Benyesh-Melnick. Fed. Proc. 28(2):698, 1969.

70-2062 PURIFIED ANTIBODIES WITH HIGH SPECIFICITY FOR SV40 TRANSFORMED HAMSTER CELL

MEMBRANES. (E.) Sulitzeanu, D. (Hebrew U. Med. Sch., Jerusalem), E. Kedar, N. Goldblum and M. Wiener. Fed. Proc. 29(2):372, 1970.

70-2063 CHRONIC VIRAL INFECTION AND ANTINUCLEAR ANTIBODY IN NEW ZEALAND MICE. (E.) Tonietti, G. (Scripps Clin. Res. Found., La Jolla, Calif.), M. B. A. Oldstone and F. J. Dixon. Fed. Proc. 29(2):492, 1970.

70-2064 IMMUNOSUPPRESSION WITH FRIEND VIRUS IN ALLOGENEIC MURINE TUMOR SYSTEM. (E.) Deodhar, S. D. (Cleveland Clin. Found., Ohio) and T. Chiang. Fed. Proc. 29(2):560, 1970.

70-2065 CYTOGENETIC STUDIES OF RAT THYMIC CULTURES TRANSFORMED BY GROSS LEUKEMIA VIRUS. (E.) Sabbath, M. (Columbia U. Coll. Physicians Surg., New York, N. Y.). Fed. Proc. 29(2):559, 1970.

See also abstract nos: 1719, 1721, 1728, 1730, 1731, 1732, 1734, 1735, 1751, 1752, 1761, 1775, 1837, 1896, 1925, 2093, 2095

0-2066 DIFFERENCES OBSERVED IN THE SITE INCIDENCE OF CANCER, BETWEEN THE PARSI COMMUNITY AND THE TOTAL POPULATION OF GREATER BOMBAY: A CRITICAL APPRAISAL. (E.) Jussawalla, J. (Indian Cancer Soc. Bombay Cancer Registry), A. Deshpande, W. Haenszel and M. V. Natekar. Int. J. Cancer 24(1):56-66, 1970.

The records of the Bombay Cancer Registry for 1964-1966 disclosed 9703 new cases of cancer, including 362 in the small Parsi community. Age-adjusted incidence rates/100,000 for all tumors combined and for several specific cancers were markedly different in the Parsis from the rates served in Greater Bombay. Rates for cancer of the oral cavity, pharynx, larynx, esophagus and cervix were lower, and rates for cancer of the breast (female), uterus, prostate, ovary and in and for all leukemias, were higher, in the Parsis than in the Bombay population. These differences were not removed by age-adjusting the data; the Parsis have an age structure very different from that of the general population, with a higher proportion of persons over 50 yr. old. Some of the differences in relative cancer rates between the Parsis and the Bombay population are attributed to environmental factors, such as their high socioeconomic status and their sanctions against tobacco smoking.

0-2067 CANCER IN THE PARSI COMMUNITY OF BOMBAY. (E.) Paymaster, J. C. (Tata Ind. Ctr., Parel, Bombay, India) and P. Gangadharan. J. Cancer 5(3):426-431, 1970.

In comparison with the population of Greater Bombay, the Parsi community shows a marked preponderance of cancer of the anterior portion of the tongue, the breast and uterus, and a low frequency of cancer of the oral mucosa, base of the tongue, cervix and lung. The low rates for cancer of the oral cavity, pharynx and lung among the Parsis were attributed to their abstention from tobacco on religious grounds. The high rate for breast cancer is discussed in relation to the relative prevalence of unmarried women, late marriages and low birth rate among the Parsis, who are also a highly inbred community. Skin cancer (with a prevalence of basal cell carcinoma) was more frequent among the Parsis than in the population of Bombay; this difference was attributed to a difference in skin pigmentation. Males showed a high incidence rate for cancer of the vocal cords and a low rate for lung cancer. Leukemias and lymphomas were more frequent than expected.

7-2068 CLINICAL OBSERVATIONS ON CANCER PATTERNS AT THE NON-WHITE HOSPITAL, AGWANATH, JOHANNESBURG, 1948-1964. (E.) Robertson, M. A. (South African Inst. Med. Res. Cancer Res. Unit, Johannesburg). S. Afr. Med. J. 4(30):915-931, 1969.

Of the pts. admitted to this hospital from June, 1948-December, 1964, 88.7% were from the Johannesburg area (excluding the Reef mines) and 95.0% were Bantus; 7817 malignant tumors (excluding precancerous lesions and noninvasive cancers), including 1 triple and 13 double primary tumors, were found. The 7316 cancers found in 1951-1964 comprised 1.3% of the 597,021 admissions; 52.4% of the cancer pts. were males. Cancer was found in 1.1% of all pts. in 1956 (48.8% were males) and 1.600% of all pts. in 1964 (57.1% were males); this change was attributed to a marked increase in esophageal cancer in males during this time. Relative frequencies of a wide variety of tumors (percentages of all admissions for each yr.) are tabulated for 1948-1964. In addition to the marked increase in esophageal cancer (males only), the data for 1958-1964 showed a slight increase in lung and bronchial cancer (especially in males); little change in cancer of the stomach, mouth and pharynx; relative decreases in cervix cancer, bone tumors and hematopoietic-lymphatic neoplasms; and a lower than expected frequency of hepatomas. A female preponderance was noted for breast and genital cancer (combined) and for thyroid cancer; male preponderances were seen for many of the other tumor types. Comparison of these data with data from the 1960 Transvaal census (25-69-yr. age group) showed that the reported sex differences among the cancer pts. were real. The census data showed 42.9% of the male population and 37.4% of the female population in the 25-69-yr. age group (57.1% of all males and 62.6% of all females were under 25 or over 70), but 79.2% of all cancers were found in the 25-69-yr. age group. Possible roles of host resistance to carcinogenic factors, as affected by genetic or constitutional components, age and sex, are discussed.

70-2069 STATUS OF ONCOLOGICAL SERVICES IN CHUVASH ASSR. (Rus.) Kuz'min, V. I. and K. K. Sidorov. Zdravookhr. Ross. Fed. 13(1):7-10, 1969.

A summary is presented of oncological services in Chuvash from 1959-1967. Data presented included proportion of the population examined, modes of treatment and morbidity and mortality rates for cancer of different sites.

70-2070 MORTALITY DIFFERENTIALS BY SOCIAL CLASS AND SMOKING HABIT. (E.) Preston, S. H. (U. California, Berkeley). Social Biol. 16(4):280-289, 1969.

A method for analyzing mortality differentials in smokers and non-smokers, as related to social class (the criterion used is educational level) is described, using data derived from several previously published studies on mortality experience among U.S. males in the 25-64-yr. age group. Males (but apparently not females) of

lower educational level seem to be more likely to smoke, and slightly more likely to smoke heavily, than male college graduates. Males with less than 8 yr. of education showed higher mortality rates from several cancers than male college graduates; the largest difference, in cancer of the stomach (the ratio between the 2 groups was 2.23:1), was tentatively attributed to dietary factors. The results of several studies suggest that the appearance of an increased mortality risk from smoking, for diseases not known to be physiologically directly related to smoking, may result from social class differences between smokers and non-smokers. Conversely, studies of mortality differences among social classes (including differences in lung cancer mortality) are probably affected by differences in smoking among these groups.

70-2071 PROSPECTIVE EPIDEMIOLOGIC STUDIES.
(Ger.) Hammond, E. C. Arch. Hyg. Bakt.
153(6):483-489, 1969.

Three prospective, American epidemiologic studies are reviewed in some detail: the Lucas County, Ohio, study of uterine cancer; the New York-New Jersey study of workers exposed to asbestos; and the American Cancer Society study of cigarette smoking, made between 1959-1964, inclusive.

70-2072 CORRELATION BETWEEN CANCER MORTALITY
AND METALLIC ION CONTENT OF CITY
DRINKING WATER. (It.) Granata, A. (U. Messina
Inst. Occup. Med., Italy), L. De Angelis, M.
Piscaglia and G. Drago. Minerva Med. 61(36):
1941-1950, 1970.

Total metallic ion content (iron, magnesium, aluminum, manganese, nickel, lead, copper, zinc, chromium, cadmium and tin, in g/liter) in drinking water of the 14 districts of Pesaro, Italy was measured twice daily and the total mean conc. compared with the cancer mortality classified at 4 levels (high, mean for the commune, below mean and very low). All water samples had iron, magnesium and aluminum; manganese was found occasionally. At group levels, a significant correlation was found between total ion conc. and cancer mortality, as well as with mortality due to cancer of the g.i. tract, liver and pancreas. The mean total ion value for the lowest value districts was 9.96 g/liter (spring water) as compared to 30.98 g/liter (well water) for high-value districts.

70-2073 CANCERS OF OTHER SITES IN PATIENTS WITH
PULMONARY TUBERCULOSIS. (Rus.)
Braude, V. I. (Sci. Res. Inst. Tuberculosis,
Moscow). Vop. Onkol. 15(4):17-22, 1969.

In a series of autopsies of 1273 pts. with pulmonary tuberculosis (TB), 344 non-TB pts. and

405 oncological pts. in the 13-yr. period 1955-1967 inclusive, the frequency and topographical characteristics of cancer of various organs were determined. Cancers were found less frequently in the TB than in the non-TB group (4.1% and 21.2%, resp.), and lung cancers were less frequent in TB pts. than in non-TB or oncological pts. (1.8% and 4.65%, resp.). However, all 3 groups showed a greater tendency for the development of extrapulmonary than pulmonary tumors. The ratio of lung cancers: all cancers was 1:5 and 1:2 for non-TB and TB pts., resp. In the TB group, there were 30 cases with extrapulmonary cancers and 23 with lung cancers; 49/53 were older than 40 yr. and they were predominantly males. Females accounted for 1/23 and 6/30 pulmonary and extrapulmonary cases, resp. In the pulmonary cases, a comparison of sites showed neoplastic and tuberculous processes in different lungs or different parts of the same lung in 18/23 cases. In the oncological group, 56/60 with lung cancer were older than 40 yr. and 58/60 were males; 1/60 (1.66%) showed TB at a different site. In the 13-yr. observation period, no increase in rate of cancers occurred in the TB pts.; it is concluded that antitubercular agents have no carcinogenic effects. Of more than 2000 TB pts. with lung resection, only 2 showed development of keratotic squamous cell carcinoma. Therefore, it is suggested that TB does not promote development of cancer; rather, there may be an "antagonism" between TB and cancer.

70-2074 THYROID CANCER IN HAWAII. (E.) Haber,
M. H. (2260 Liliha St., Honolulu, Haw.)
and P. Lipkovic. Cancer 25(5):1224-1227, 1970.

Records for 1962-1966 from 5 hospitals of Oahu (comprising 82% of the hospital beds on Oahu) disclosed 158 cases of thyroid carcinoma among residents of Oahu (excluding military personnel). The female:male ratio was 3:1. Av. annual age-standardized incidence rates/100,000 (world standardized) for thyroid cancer (3.5/100,000 for males and 9.7/100,000 for females) were the highest in the world for females and the second highest for males. In all 5 ethnic groups studied, rates were higher than in comparison populations: 3.1 in male and 10.3 in female Caucasians (compared to 1.2 and 3.1, resp., in Connecticut); 2.2 in male and 5.5 in female Japanese (compared to 1.1 and 2.6, resp., in Miyagi, Japan); 6.3 in male and 17.6 in female Chinese (compared to 0.5 and 1.0, resp., in Singapore Chinese); 5.0 in male and 9.6 in female Filipinos; and 7.0 and 10.6, resp., in Polynesians. There is no apparent iodine deficiency in Hawaii, and endemic goiter is rare. Radiation exposure is suggested as a possible etiologic factor. Crude data on thyroid cancer occurrence, collected after the end of this study, suggest that the thyroid cancer incidence rate is presently increasing in Hawaii.

-2075 SURVIVAL RATES OF NASOPHARYNGEAL CANCER IN CALIFORNIA. A REVIEW OF 516 CASES FROM 1942 THROUGH 1965. (E.) Schnohr, P. ratmosevej 24, Vedbaek, Denmark). Cancer (5):1099-1106, 1970.

The California Tumor Registry records for 1942-1965 (inclusive) disclosed 516 primary cancers of the nasopharynx, including primary carcinomas of 343 Caucasian and 67 Chinese pts. Primary carcinomas of the nasopharynx comprised 0.1% of all reported tumors in Caucasians and 6.6% in Chinese during this period. The Chinese:Caucasian ratio in the population of California is about 1:600, but among pts. with nasopharyngeal cancer was about 1:20. Male:female ratios among the Caucasian and Chinese pts. were 2.4:1 and 4.2:1, resp. Av. ages at diagnosis in Caucasians and Chinese were 55.3 and 46.4 yr., resp., in males, and 55.1 and 46.0 yr., resp., in females. The earlier age at diagnosis among the Chinese was greater than the mean age differences observed between the populations, for both sexes. Survival rates were better in females than in males, and better in the younger age groups than in the older groups. In both groups, females showed fewer remote and regional cancers and more localized cancers than males.

-2076 CLINICAL PICTURE AND DIFFERENTIAL DIAGNOSIS OF MALIGNANT MELANOMA. (E.) Schnyder, U. W. (U. Heidelberg Derm. Clin., Germany). Schweiz. Med. Wschr. 100(23):3-966, 1970.

Incidence, pathogenesis, clinical picture, differential diagnosis, laboratory diagnostic methods, course and prognosis of malignant melanoma are briefly reviewed. In Switzerland the annual number of reported deaths due to malignant melanoma increased from 56 (1.1% of all deaths) in 1951 to 97 (1.7%) in 1963. In addition to the skin, malignant melanoma occurred in the eyes, brain and internal organs. Among 4 fatal cases in Switzerland (1962-1963), it was located in the skin in 145 (83%), eyes in 12 and other organs in 5. In the remaining 12 cases, the primary site was not determined.

-2077 FAMILIAL OCCURRENCE OF MALIGNANT MELANOMAS. (Nor.) Grimstvedt, M. (Strandgt. 113, Haugesund, Norway). T. Norsk. Lægeforen. 89(24):1900-1902, 1969

In a family studied in 1969, the mother was known to have died of malignant melanoma (skin and intraabdominal tumors) in 1936. Malignant melanoma also developed in 2/3 daughters (aged 41 and 49 yr.) and 3/5 sons (32, 47 and 51 yr. old); 2 of several grandchildren showed initial signs of the disease at ages 17 and 19 yr. The mother (age 82 yr.) remains well with no signs of disease or familial history of melanoma. Although the criteria for a dominant autosomal

gene are satisfied, it is suggested that the locus of the dominant gene could be the maternal X chromosome.

70-2078 CANCER OF FEMALE GENITALIA IN KIROVABAD. (Rus.) Mamedov, I. M. (Kirovabad Oncol. Dispensary, USSR). Vop. Onkol. 15(7):100-102, 1969.

In Kirovabad and its 4 districts, 250 cases of female genital cancer were recorded from 1960-1966. Cancer of the cervix (CC) accounted for 74.7% of all gynecological cancers; for uterus (UC), ovaries, and vulva and vagina, the distribution was 13%, 7.1% and 5.2%, resp. For the 6-yr. period, distribution of morbidity rates/100,000 female population ranged from 18-48.3, according to ethnic group (Azerbaijani, Armenian, Russian, etc.). The ratio of CC:UC for all women studied was 1:5.5. Incidence of genital neoplasms for the 1960-1966 period in Kirovabad was 29.3/100,000 females.

70-2079 LACTATION AND REPRODUCTIVE HISTORIES OF BREAST CANCER PATIENTS IN GREATER ATHENS, 1965-67. (E.) Valaoras, V. G. (U. Athens), B. MacMahon, D. Trichopoulos and A. Polychronopoulou. Int. J. Cancer 4(3):350-353, 1969.

A study was made of 700/956 women resident in Athens, Piraeus and suburbs diagnosed as having breast cancer between January 1, 1965 and June 30, 1967, along with 2,470 controls. Incidence rates peaked in the 50-54-yr. age group (at about 100/100,000/yr.), leveled off, then declined after age 70. Trends toward a higher incidence were seen in married women (attributed to an artifact), in those of higher socioeconomic levels, in those having earlier menarche and in those having a later menopause. Little difference in incidence was observed between parity 0 and parity 2, but a 50% decrease in incidence was seen for parity 5 or more; there was also a 2-fold greater risk among women pregnant for the first time over age 30 as compared to those under age 20, and in taller and heavier women as compared to shorter and lighter ones. No significant correlation was found with lactation experience, contraceptive use, regularity of menstrual periods or breast size.

70-2080 TWO EPIDEMIOLOGICAL TYPES OF BREAST CANCER. (Ger.) Berndt, H. (Robert Rossle Clin., Berlin) and R. Landmann. Arch. Geschwulstforsch. 33(2):157-168, 1969.

A retrospective study of 1039 breast cancer pts. treated between 1949-1964 at the Robert Rössle Clinic in Berlin and 1065 controls (pts. with g.i., gynecological, liver and gallbladder, thyroid and blood diseases) divided into groups (I: 5 yr. before, II: up to 5 yr. after, III:

5-10 yr. after, and IV: 10 or more yr. after menopause) revealed the following: breast cancer pts. (all groups) more frequently had mothers who also had breast cancer, more frequently were single, married later in life, had fewer children and nursed them for a shorter period of time, more frequently had a pyknic body build, were overweight and had high blood pressure. Contrary to a previous report, they had no increased frequency of ovarian and uterine disease when compared to controls. Two epidemiological types of breast cancer were differentiated: a premenopausal (group I) and late postmenopausal (group IV); tumors in group II belonged partly to the pre- and partly to the postmenopausal type. Benign breast tumors and different mammary gland diseases were significantly more frequent in group I than in controls (but not in II, III, or IV). Thyroid diseases, which were more frequent in cancer pts. of all groups than in controls, showed a higher incidence in groups I and II than III and IV. Compared to controls, only postmenopausal groups III and IV showed a higher incidence of liver and gall-bladder diseases. Pyknic body build, obesity and hypertension were more frequent and more pronounced in postmenopausal groups II, III and IV than in Group I. It is suggested that the premenopausal type could be related to disturbance in the regulatory mechanism of the pituitary while the postmenopausal type could be due to mild hyperfunction of the adrenal cortex.

70-2081 SOME OBSERVATIONS ON OESOPHAGEAL CARCINOMA IN CEYLON, INCLUDING ITS RELATIONSHIP TO BETEL CHEWING. (E.) Stephen, S. J. (Gen. Hosp., Ratnapura, Ceylon) and C. G. Uragoda. Brit. J. Cancer 24(1):11-15, 1970.

Epidemiologic data were studied for 237 pts. with carcinoma of the esophagus, admitted to 2 hospitals in Ceylon (Ratnapura and Kandy). Betel chewing was admitted by 90/111 pts. questioned (81.1%). A survey of the population of 1 of the communities (Kandy) showed a much lower prevalence of betel chewing (328/1088 persons, or 30.1%). The pt. group was preponderantly female (138/237 pts., or 58.6%). The av. age at diagnosis was 46.9 yr. in the women and 52.5 yr. in the men; 23.2% of the women and only 10% of the men were under 40 yr. of age at diagnosis. The middle third of the esophagus was the primary tumor site in 55.7%, the lower third in 33.3% and the upper third in 11.0%. At all 3 tumor sites, the incidence was higher in females than in males. The frequency of betel chewing in the population of Kandy was higher in females than in males (32.3% and 27.9%, resp.). Since Ceylonese women seldom smoke tobacco or drink alcoholic beverages, the high frequency of esophageal cancer among Ceylonese women was attributed to betel chewing. It is noted that oral cancer, which has also been considered to be associated with betel chewing, is the most common malignant tumor in Ceylon (in the 12-mo. period 1965-1966,

the incidence rate for all of Ceylon was 28.3/100,000 population).

70-2082 CANCER OF THE OESOPHAGUS: FURTHER EVIDENCE OF THE RELATION TO DRINKING HABITS IN FRANCE. (E.) Tuyns, A. J. (Int. Agency Res. Cancer, Lyons, France). Int. J. Cancer 5(1):152-156, 1970.

Age-specific annual mortality rates (1960-1963) for esophageal cancer, alcoholism and liver cirrhosis, in males aged 45-64 yr., were analyzed for the 88 departements and 21 regions of France. Significant positive correlations were found between esophageal cancer and alcoholism and between esophageal cancer and cirrhosis. All of the departements showing cancer mortality rates of 50/100,000 or more also showed alcoholism mortality rates of at least 70/100,000; these departements were all in western France. In Haute-Savoie, Savoie and Ardennes, however, the cancer mortality rates were "normal" (30-40/100,000) while the alcoholism mortality rates were high. Since acute or chronic alcoholism (related to distilled liquors) showed a higher correlation with cancer of the esophagus than did liver cirrhosis (related to wine or beer), it is suggested that the carcinogen(s) responsible for this tumor may require conc. alcohol as a vehicle. It is also suggested that the carcinogen(s) may be present in liquors consumed in some areas of France (notably western France) but not in other areas such as Savoie.

70-2083 CHRONOLOGICAL STUDY OF STOMACH CANCER. (Ic.) Sigurjónsson, J. Laeknabladid 55(4):117-127, 1969.

In Iceland from 1921-1965, while the incidence of cancer in general increased (from 121 to 140/100,000), the incidence of stomach cancer decreased (from 45 to 39/100,000). Cancer of the stomach was more frequent in males, increased with age and varied geographically, being 25.5% greater in northwestern Iceland than in the rest of the country, and less in urban than rural areas. Frequency was greatest for farmers and laborers; it was seen among sailors, tradesmen and professional men in descending order. Frequency was correlated to the 3,4-benzpyrene (BP) content in the diet. Meat and fowl singed or smoked over coal or peat fires contained about 20 µg/kg BP as compared to less than 1 µg/kg when singed by propane or acetylene-oxygen flame. Thus, home-smoked meat has much more BP than commercially prepared meat. Seabirds singed by "old methods" have a very high BP conc. (no details).

70-2084 PRIMARY CARCINOMA OF THE LIVER IN ETHIOPIA. A STUDY OF 38 CASES PROVED AT POST-MORTEM EXAMINATION. (E.) Pavlica, D. (Imperial Ethiopian Armed Forces Hosp., Addis

baba) and I. Samuel. Brit. J. Cancer 24(1): 2-29, 1970.

Chronic liver disease was diagnosed in 236/2880 adults admitted to an Ethiopian hospital in 1966-1968. The 38 primary liver carcinomas (all hepatocellular type) noted during this time caused 20% of all deaths in the hospital. The number of males exceed that of females (35:5) and most of the pts. (74%) were 41-60 yr. old. Cirrhosis was seen in almost all, 36/38 (94.7%); 7/36 showed postnecrotic cirrhosis. No fatty changes, nutritional cirrhosis or liver parasites were noted. The high frequency of postnecrotic cirrhosis suggests the importance of a hepatotoxic etiologic factor. All pts. reported regular use of indigenous plant preparations as remedies against intestinal Taenia infestations; possible effects of these hepatotoxic taenicides and of dietary mycotoxins as carcinogens are discussed.

20-2085 INCIDENCE AND MORTALITY OF INTESTINAL CANCER. (E.) Ashley, D. J. B. (Morrison Hosp., Swansea, Wales). Cancer 25(4):959-965, 1970.

Age-specific incidence and mortality rates for cancer of the colon and rectum (England + Wales and the U.S.) were examined. The results were in agreement with the "multiple-hit" theory of carcinogenesis, except that the postulated number of "hits" was one greater for the mortality rate than for the incidence rate. It is suggested that this additional "hit" confers the property of "aggressiveness" on the tumor, either during the process of carcinogenesis or during the progression of an established tumor. In carcinoma of the stomach and pancreas, the same number of "hits" are required for the observed incidence and mortality curves.

20-2086 A SYSTEMATIC SEX DIFFERENCE IN INTESTINAL CARCINOMA. (E.) Ashley, D. J. B. (Morrison Hosp., Swansea, Wales). Cancer 25(4):966-971, 1970.

Several sets of data on colon and rectum cancer mortality from England and Wales and from the U.S. were used to prepare age- and sex-specific mortality rates. Deaths from cancer of the colon were about equal in males and females; the number of deaths from cancer of the rectum was greater in males than in females. When age-specific incidence rates were plotted in double logarithmic form, the rates fell on straight lines, but the line was steeper for men than for women. This was observed for both tumor types. The data suggested that the number of "hits" required for tumor development was one higher in males than in females. The possibility that the additional "hit" might involve the Y chromosome is considered unlikely; it is suggested that a sex difference in susceptibility may result from the action of dominant genes present on the X chromosome.

70-2087 PRIMARY MALIGNANCY IN PATIENTS UNDERGOING IMMUNOSUPPRESSION FOR RENAL TRANSPLANTATION. A REQUEST FOR INFORMATION. (E.) McKhann, C. F. (U. Minnesota Hosp., Minneapolis). Transplantation 8(2):209-212, 1969.

In 1968 a questionnaire was sent to all surgeons contributing to the Transplantation Registry and incidence of tumor development under immunosuppressive therapy was examined to determine if some human tumors may be antigenic, as evidenced by their appearance in increased numbers in the absence of normal immune response. Transplant cases were considered only if the donor showed no evidence of tumor. The incidence rate for malignancy was 13/2000 kidney transplant pts., compared to 8.2/100,000 for the general population under 40 yr. of age. More than half of the tumors were primary tumors of the RES, especially reticulum cell sarcoma (4 cases). No other tumor has yet appeared more than once. It is suggested that the development of these RES tumors may be a direct result of toxic action on the RES by one of the agents used. The need for additional information on the interrelationship between immunosuppressive therapy and malignancy is stressed.

70-2088 SYMPATHICOGONIOMAS AND HEREDITY OF MALIGNANT TUMORS. (Ger.) Ullrich, R. (St. Georg Reg. Hosp. Path. Bact. Inst., Leipzig, Germany). Schweiz. Med. Wschr. 100(17):749-751, 1970.

Neuroblastoma sympathicum is reported in 2 boys who died at age 18 mo. and 4.5 yr., resp. In 1, born with a tumor on the neck, the diagnosis of sympathicogonioma originating from the cervical sympathetic nerve was made soon after birth; for the other boy, diagnosis of sympathicoblastoma originating in the medulla of the right adrenal gland was made at age 4 yr. 2 mo. Both cases showed massive metastases, especially to the liver. Both maternal and paternal sides of the families of the 2 distantly-related (grandmothers were second cousins) children had a high incidence of a wide variety of cancers; 7/41 and 8/47 family members, resp., died of cancer, many at an early age.

70-2089 CONNECTION BETWEEN THE RATE OF SKELETAL GROWTH AND APPEARANCE OF OSTEOGENIC SARCOMA. (Rus.) Solov'ev, Iu. N. (Inst. Exp. Clin. Oncol., Moscow). Vop. Onkol. 15(5):3-7, 1969.

Analysis of age-sex distribution of 112 pts. (74 males, 38 females; 7-57 yr. old) treated for primary osteogenic sarcoma (OS) from 1955-1966 demonstrated a significantly high frequency (59%) in the 11-20-yr. age group, with higher prevalence among males than females. In 72 pts. (7-35 yr. old) with OS of long bones observed from 1957-1966, the highest frequency occurred

in the 11-20-yr. age group; frequency was greatest in females aged 11-15 yr. and males ages 16-20 yr. Tumors were localized in the knee joint in 75% pts. A possible relationship between development of OS and age-increased growth processes and skeletal reorganization is suggested.

70-2090 OCCURRENCE OF MALIGNANT PRIMARY TUMORS OF THE LIMBS AND EXTREMITIES IN THE POPULATION OF 11 DISTRICTS. (Ger.) Blankenburg, H. (Stavenhagen Hosp., Germany). Beitr. Orthop. Trauma. 17(1):31, 1970.

Between 1955-1967, inclusive, the number of reported cancers in the German Democratic Republic ranged from 2.21-3.45% of the total population each yr., while new cases of tumors of the bone and cartilage represented 0.4-0.5% of all such reported malignancies. Plasmocytomas represented 0.3-0.4%. During the past 20 yr., a total of 101 malignant tumors of the limbs and extremities was reported in 11 of the country's districts, among a total population (date not specified) of 534,137. Included (male:female ratios in parentheses) were 25 polymorphocellular sarcomas (12:13), 15 plasmocytomas (2:3), 12 osteosarcomas (2:1), 11 fibrosarcomas (4:7), 10 spindle-cell sarcomas (1:1), 8 reticulum-cell sarcomas (5:3), 6 chondroosteoplastic sarcomas (2:1), and 2 cases, each, of Ewing's (0:2), myxochondrooste- (0:2), fibromyxo- (0:2), myxo- (1:1) and angiomyxolipo- (0:2) sarcomas, as well as 2 giant-cell tumors (0:2) and 1 case, each, of chordoma and angiosarcoma (both in males). Both Ewing's sarcomas were in girls under 10 yr. of age.

70-2091 MALIGNANT LYMPHOMA IN THE SAUDI ARAB. (E.) Gelpi, A. P. (Stanford U. Sch. Med., Calif.). Cancer 25(4):892-895, 1970.

From 1953-1967, 43 pts. with malignant lymphomas were seen at the Dhahran Health Center (which serves a large population living along the Persian Gulf, including employees of the Arabian American Oil Company and their dependents). These 43 pts. included 39 males and 4 females; 12/43 were children (aged 20 mo.-14 yr.). Hodgkin's disease was found in 15/43 (35%), lymphosarcoma in 23/43 (53.4%) and reticulum cell sarcoma in 5/43 (11.6%). Eighteen pts. (41.8%) presented with primary abdominal lymphoma; an additional 16 had abdominal involvement when first seen. The most frequently affected sites were the jejunal, ileal and mesenteric lymph nodes. This high frequency of primary abdominal lymphoma among Saudi Arabs corresponds to data previously reported for other populations of the same ethnic background (such as Arabs and Sephardic Jews in Israel), suggesting the existence of a common environmental or ethnic factor.

70-2092 A SURVEY OF MALIGNANT LYMPHOID TUMORS AMONG IRANIANS. (E.) Armin, K.

(Teheran U., Iran). Acta. Med. Iran. 11(1-2): 35-62, 1968.

Examination of 68,000 biopsy specimens, obtained from all parts of Iran over a 25-yr. period, disclosed primary lymphoid tumors (excluding leukemias) in 1368/5814 lymph node biopsies (23%), tuberculosis in 2335/5814 (40%), and other lesions in 2111/5814 (36%). An autopsy series (obtained over the same 25-yr. period) included 366/1917 with malignant tumors, including 81 primary lymphoid tumors. Lymphosarcomas, reticulum cell sarcomas and giant follicular lymphomas comprised 60.5% of the 1368 primary lymphoid tumors. The male:female ratio in these 828 pts. was 2.5:1. The age range at diagnosis was 2-75 yr.; the largest number of pts. was in the 25-35-yr. age group. Extranodal initial manifestations were seen in 150/828. Almost 33% of the children under 10 presented with intra-abdominal tumors; many of the 28 pts. with reticulum cell sarcomas were in the 10-20-yr. age group. One child had a Burkitt lymphoma-like reticulum cell sarcoma of the maxilla and ovaries. Hodgkin's disease and related disorders (ranging from simple lymphoid hyperplasia to lymphoreticular hyperplasia in 73 pts.) comprised the remaining 39.5% of the 1368 lymphoid tumors. The male:female ratio in this group was 3.5:1. The group included 38/540 children under 15 (7%) and 38 pts. over 65; the largest age group (at the time of diagnosis) was the 25-35-yr. age group. Unusual primary tumor sites were noted in 39/540 with Hodgkin's disease.

70-2093 EPIDEMIOLOGIC STUDIES OF CHILDHOOD LEUKEMIA IN GREEN BAY, WISCONSIN. (E.) Flynt, J. W., I. L. Doto, R. J. McCollough and T. D. Y. Chin (Nat. Communicable Dis. Ctr., Kansas City, Kan.). J. Nat. Cancer Inst. 44(3): 489-495, 1970.

All cases of leukemia, lymphoma and congenital defects in the metropolitan area of Green Bay, Brown County, Wisconsin were studied after a cluster of 5 cases of acute lymphocytic leukemia was found there in 1963 and 1964. Incidence rates for children less than 5 yrs. of age with leukemia for 1958-62 and 1963-64 were 19.2 and 27.4/100,000, resp., while the mean state-wide death rate for the same age group in 1960-63 was 5.8/100,000. Most leukemia cases occurred in western Green Bay, but this was not attributed to any significant difference between the eastern and western sections of the city. All 5 cases in the cluster occurred in western Green Bay. The occurrence of adult leukemias and lymphomas for 1958-66 showed that both eastern and western sections of the city were comparable in incidence. Between 1961 and 1966, 158 infants were born with congenital defects; the rate of defects was highest in 1963 (11/1,000 live births). November and December, 1963 had the peak number of 11 malformed infants; 2 children had onset of acute leukemia during this period.

-2094 TIME BETWEEN PAIRS OF LEUKEMIA CASES.
(E.) Bailar, J. C., III (NCI, Bethesda,
), H. Eisenberg and N. Mantel. Cancer
(6):1301-1303, 1970.

ta on 4552 leukemias reported in Connecticut
1935-1963 (inclusive) were examined for time
comparisons from 1 case to another in the same
all geographic area. No clear evidence was
found that such cases tend to occur at fixed time
intervals; such spacing was not seen even after
separate analyses of case occurrence according
age group or community size.

7-2095 OUTBREAKS OF LEUKEMIA IN JAPAN. (Jap.)
Kobayashi, H. (Hokkaido U. Sch. Med.
Cancer Inst., Sapporo, Japan) and K. Kamibayashi.
Haemat. (Jap.) 31(5):810-817, 1968.

ta obtained over a 5-yr. period (1962-1966)
from 3288 Japanese communities were studied, to
detect temporal and/or spatial clustering of
leukemia deaths, in addition to 2 clusters
previously reported in Shizunai (Hokkaido) and
Sakawa (Gifu prefecture). The observed fre-
quency of towns (stratified into several groups
according to population) with zero or 5 leukemia
deaths each was significantly above the expected
frequency (Poisson distribution) and was fairly
close to a Polya distribution. Ederer's method
was used to study temporal clustering of leukemia
deaths in all cities and towns of Japan. A 1-yr.
clustering, significant at the 5% level, was
observed for all of Japan; a cluster significant
at the 1% level was noted in the Kyushu region.
Few towns with new leukemia outbreaks (less
than 0.5% Poisson distribution, at the 1% level
of significance) were noted in Ryozen (Fukushima
prefecture), Kabe (Hiroshima prefecture; 2/5 of
these pts. had been exposed to the atomic bomb),
Yato (Saga prefecture) and 2 towns in Nagasaki
prefecture (Saishi and Kunimi). The leukemia
outbreak in Shizunai occurred 1 yr. after an
outbreak of rubella. Antibodies reacting to
leukemia brain antigen (in the passive cutaneous
anaphylaxis test) were found in sera from members
of the families of leukemia pts. from Shizunai,
but not from the pts. themselves or from other
healthy residents of Shizunai. A significant
difference was found, suggesting the existence
of some specific agent in leukemia pts. in the
outbreak area. Possible etiologic factors are
discussed, with particular reference to viruses.

7-2096 STUDY OF THE AGE OF ONSET ON THE
ETIOLOGY AND PATHOLOGY OF NEOPLASIA.
(I.) Soini, A. (20079 S. Angelo Lodigiano,
Milan, Italy) and F. D'Angostino. Minerva Med.
63(6):1951-1967, 1970.

In a study of about 6000 pts. from the Poly-
clinic and Greater Hospitals of Milan from 1954-
1965, the significance of age at onset of cancer
of the various organs was determined. Results

were similar to those of other investigators;
that is, the risk of epithelial tumors and
carcinoma for all sites increases with age. It
is suggested that the evolution of neoplasms is
due to factors with thresholds of action which
are reached with increasing frequency later in
life. Also, factors associated with cell
senescence possibly are important in the
relationship between age and carcinogenesis.

70-2097 AN INBRED LINE OF SYRIAN HAMSTERS WITH
FREQUENT SPONTANEOUS ADRENAL TUMORS.
(E.) Homburger, F. (Bio-Res. Inst., Cambridge,
Mass.) and A. B. Russfield. Cancer Res. 30(2):
305-308, 1970.

Syrian hamsters of inbred lines B10 4.24 and
45.5 were sacrificed at various intervals and
examined histologically. There were 30 adrenal
tumors in 24/53 strain 4.24 hamsters and 8
adrenal tumors in 6/35 strain 45.5 hamsters.
Amyloidosis of the adrenal glands was seen in
about 26% of line 4.24 and in about 37% of line
45.5. In line 4.24, the av. age of tumor-bearing
males and females was 92 and 94 weeks, resp., as
compared to 68 weeks and 64 weeks, resp., for
non-tumor-bearing animals. The tumor-bearing
animals were also older in the other strain.
Males of both lines had a similar incidence of
tumors (33 and 25%), while 61% of strain 4.24
females had adrenal tumors as opposed to 6.7%
of females in the low-tumor line. It is
suggested that genetic factors account for the
highly variable occurrence of spontaneous
adrenal tumors in hamsters.

70-2098 STATISTICAL DATA ON NEOPLASTIC
DISEASES IN DOGS IN MOSCOW (1962-1966).
(Rus.) Orlova, L. V. (Inst. Exp. Clin. Oncol.,
Moscow) and P. E. Terekhov. Vop. Onkol. 15(4):
91-95, 1969.

Primary tumors were found in 1200/12,000 dogs
treated for various non-infectious diseases in
Moscow from 1962-1966; 828/1200 (69%) were
females and 372 (31%) were males. Mammary
tumors comprised 31.5% of the total (371 females,
7 males) and were confirmed histologically in
28% of the group. Skin tumors comprised 20.4%
of all tumors found (105 females, 140 males);
bone tumors comprised 11.1% (73 females, 60
males). Venereal sarcomas (10.2% of all tumors)
were found in 83 females and 40 males, and
other genital tumors (2.8% of all tumors) in 16
females and 18 males. Generally, the frequency
of the mammary tumors and the venereal sarcomas
increased and decreased, resp., in dogs aged 0-13
yr., and decreased for both thereafter. Among
pure-bred dogs, a high proportion of mammary
tumors were found among Eastern European sheep-
dogs, hunting dogs and "ornamental" dogs.

70-2099 MATHEMATICAL ANALYSIS OF THE ESTABLISHMENT OF HUMAN PERIPHERAL BLOOD CELL LINES. (E.) Rosenfeld, C. (Inst. Cancer Immunogenet., Villejuif, France) and A. Macieira-Coelho. J. Nat. Cancer Inst. 43(3):597-602, 1969.

Cell lines established from normal and leukemic human peripheral blood cells showed similar growth patterns, including an initial decline in cell number, an inflection, then a rise in cell number. The percentage of cells synthesizing DNA was measured by placing cultures in a medium containing $1 \mu\text{C}/\text{ml}$ ^3H -thymidine. Mathematical analysis rejected the theory of 2 populations existing at the start of the culture and supported the theory of a single population having an original increase in cell death, then a decrease in cell death with the appearance of proliferating cells, and finally, a linear increase in the total cell number. A general mathematical law for the establishment of WBC cultures was presented.

70-2100 THERAPEUTIC IMPLICATIONS FROM A MATHEMATICAL MODEL CHARACTERIZING THE COURSE OF BREAST CANCER. (E.) Slack, N. H. (Roswell Park Mem. Inst., Buffalo, N. Y.), L. E. Blumenson and I. D. J. Bross. Cancer 24(5): 960-971, 1969.

A mathematical model characterizing the course of human breast cancer is described. Testing of this model against data from clinical trials (First and Second National Surgical Adjuvant Breast Projects) indicated the existence of 2 types of breast cancer: Type A, comprising about 20% of the population, with a 2-fold faster doubling time, a shorter delay in time for the pt. report of the disease, a higher risk of nodal involvement and a higher risk of occult metastases at the time of surgery; and Type B, a slow-growing form. These results were related to developing a more effective therapeutic approach.

See also abstract nos: 1712, 1719, 1721, 1723, 1726, 1733, 1739, 1742, 1743, 1748, 1755, 1756, 1757, 1763, 1781, 1791, 1806, 1824, 1909, 1967, 1969, 1970, 2037, 2038, 2039, 2043, 2050, 2101, 2105, 2108

0-2101 STUDY OF MALIGNANT TRANSFORMATION IN TISSUE CULTURE BY THE MICROFILM METHOD. (Rus.) Ruchkovskii, B. S. (Kiev Sci. Res. Inst. Exp. Clin Oncol., USSR) and V. A. Shuklinov. Op. Onkol. 15(4):52-55, 1969.

Spontaneous malignant transformation of normal rat fibroblasts during cultivation *in vitro* was studied by microfilm. During week 1 of cultivation, cells showed active transfer, grouping, formation of islets, change in size, localization without orientation and, sometimes, passage from cell to cell with subsequent joining of cytoplasm. Further passages showed the tendency of cells to aggregate and form a layer with their processes in the same direction. After 1-3 mo., growth was delayed and mitosis was rare. After 4 mo., large irregular cells appeared and mitosis, as well as the number of nucleoli and cytoplasmic inclusions, increased. Development of polymorphic cells, atypical mitosis and large multinuclear cells was noted at 9-10 mo. At the same time, transfer and rotary movement of nuclei was stimulated. Transplantation of cells (1 ml suspension with $1-1.5 \times 10^6$ cells, s.c.) resulted in development of spindle cell sarcomas at the site of inj. in 19/30 rats.

0-2102 APPEARANCE OF GLANDLIKE STRUCTURES IN THE TRACHEOBRONCHIAL TREE OF AGING MICE. (E.) Nettesheim, P. (Oak Ridge Nat. Lab., Tennessee) and D. H. Martin. J. Nat. Cancer Inst. 44(3):687-693, 1970.

Histopathological study of the respiratory tract showed the level of the thyroid was performed on specific-pathogen-free (SPF) C57BL/6 and BC3F₁ mice (7 weeks, 3-4 mo., 7 mo. and 24 mo. old), F3H, germfree C3H and RFM, and conventional M mice (all 12-18 mo. old). Young, 7-week-old animals had no mucus-producing glands in the lower trachea or bronchi, whereas some glandlike structures were seen in 3-mo.-old mice. In 7-mo.-old animals, they were more frequent in the trachea, but never seen in the bronchi. The 12-mo.-old mice had regular numbers in all portions of the trachea and bronchi. A small number of cells had strongly periodic acid-Schiff (PAS)-positive structures, many in the distal trachea and stem bronchi. It is concluded that the appearance of these structures in conventional and SPF, as well as germfree mice, shows that inflammatory processes are not necessary for tracheobronchial gland development.

0-2103 OBSERVATIONS ON AN UNUSUAL ENZYME DISTRIBUTION PATTERN IN THE COLON OF A CASE OF FAMILIAL POLYPOSIS WITH MALIGNANT CHANGES. (E.) Maggi, V. (Imperial Cancer Res. Fund, London) and A. P. Wyatt. Gut 11(4):319-322, 1970.

Enzyme analysis was made of a specimen from a 43-yr.-old woman with rectal carcinoma who died with hepatic metastases, coming from a known polyposis family. Her mother, grandmother and aunt had died of large intestine carcinomas and polyposis was diagnosed in a son. In comparison to normal mucosa, enzyme activity in carcinoma cells was decreased and randomly distributed. Whereas alkaline phosphatase was found only in capillaries of the normal mucosa, in carcinomatous tissue it was in capillaries, smooth muscle cells and cells of epithelial origin. Acid hydrolases, esterases and β -glucuronidase were active at the base of epithelial, lamina propria and muscle cells.

70-2104 THE COINCIDENCE OF NEUROBLASTOMA AND ACUTE CEREBELLAR ENCEPHALOPATHY. (E.) Bray, P. F. (U. Utah Coll. Med., Salt Lake City), F. A. Ziter, M. E. Lahey and G. G. Myers. J. Pediat. 75(6, Pt. 1):983-990, 1969.

An association between development of neuroblastomas in children and symptoms of acute cerebellar encephalopathy (ACE) is reported in 3 case histories and for 6 other pts. in the literature. Although the etiology of ACE is unknown, it is suggested that neuroblastomas are the cause of cerebellar symptoms such as ataxia, opsoclonus and impaired brain function. It is suggested that, for all cases of ACE, a complete search for evidence of neuroblastoma be performed.

70-2105 COINCIDENCE OF CONGENITAL MALFORMATION AND EMBRYONIC TUMOURS OF CHILDHOOD. (E.) Berry, C. L. (Inst. Child Health, London), J. Keeling and C. Hilton. Arc. Dis. Child. 45(240):229-231, 1970.

A study of congenital malformations and embryonic tumors (nephroblastomas, hepatoblastomas, teratomas and neuroblastomas) in childhood showed no significant association between the two disorders for the cases observed at The Hospital for Sick Children, London. The excessive incidence of abnormalities with sacrococcygeal teratoma indicates a possible relationship of tumor to local growth processes; for these examples, the tumor masses were present at birth.

70-2106 A SYNDROME OF PSEUDOHERMAPHRODITISM, WILMS' TUMOR, HYPERTENSION, AND DEGENERATIVE RENAL DISEASE. (E.) Drash, A. (Child. Hosp., Pittsburgh, Pa.), F. Sherman, W. H. Hartmann and R. M. Blizzard. J. Pediat. 76(4):585-593, 1970.

The presence of Wilms' tumor is studied in 2 unrelated children with abnormalities of sexual

differentiation and who died of uremia due to degenerative renal disease associated with hypertension. One child had a typical 6.0 cm Wilms' tumor of the right kidney (discovered early in the course of observation) and the other a well circumscribed, encapsulated Wilms' tumor in the upper pole of the right kidney (discovered at postmortem). Deterioration in renal function was not related to the presence of the tumor. An increased incidence of Wilms' tumor is postulated for pseudohermaphroditism.

- 70-2107 CONGENITAL HYPOGAMMAGLOBULINEMIA PRECEDING HODGKIN'S DISEASE: A CASE REPORT AND REVIEW OF THE LITERATURE. (E.) Gellman, E. F. (Washington U. Sch. Med., St. Louis, Mo.) and T. J. Vietti. J. Pediat. 76(1): 131-133, 1970.

Hodgkin's disease was diagnosed in an 11-yr.-old boy with congenital hypogammaglobulinemia, which had been diagnosed 7.5 yr. previously. A history of repeated infections, especially of the respiratory tract, is implicated in the production of potentially malignant cells.

- 70-2108 DERMATOGLYPHICS IN RETINOBLASTOMA. (E.) Vidal, O. R. (Inst. Biol. Exp. Med., Buenos Aires, Argentina), A. Damei and J. Cordero Funes. J. Genet. Hum. 17(1/2):99-106, 1969.

Dermatoglyphic analysis of 4 girls and 6 boys (ages 3-6 yr.) with retinoblastomas showed 9/10 with abnormalities of the hand lines. Compared to controls (40 university students with no congenital malformations), the pts. had a significantly larger Penrose angle, an elevated axial triradius, a larger percentage of ulnar loops and whorls in the hypothenar area and transversality of the distal crests.

- 70-2109 PALMAR AND PLANTAR SEED KERATOSES AND INTERNAL MALIGNANCY. (E.) Rhodes, E. L. (Kingston Hosp., Surrey, England). Brit. J. Derm. 82(4):361-363, 1970.

In a study of pts. age 40 yr. or over attending a skin clinic, 308/500 (62%) had seed keratoses on the palms, soles or both. Keratoses were seen in 249/411 (61%) pts. without cancer and in 59/89 (66%) of those with cancer (including 58 cases of basal cell epithelioma). Studies of the frequency of cancer in families of pts. and frequency of keratoses in males and females showed no significant difference. It is concluded that development of seed keratoses has no significant association with cancer. Also, pressure or weight have no effect on location of keratoses, and the role of arsenic intake on their development cannot be determined.

- 70-2110 ON THE PATHOGENESIS OF GASTRIC ULCER IN THE AGED AND ON THE ANTAGONISM BETWEEN CALCIFIED ATHEROSCLEROSIS AND GASTRIC CARCINOMA: A RADIOLOGICAL STUDY. (E.) Elkeles, A. (39 Devonshire Place, London). J. Amer. Geriat. Soc. 18(6):450-457, 1970.

In a study of pts. aged 50 yr. to over 80 yr., there were 224 cases of carcinoma of the stomach, 330 of chronic primary gastric ulcer and 1,704 controls. Radiography of the abdominal aorta was performed to classify pts. with calcified atherosclerosis. Frequency of atheroma was greatest for the gastric ulcer group, was less for controls, and it was least for those with stomach carcinoma. For males, the frequency of primary gastric ulcer peaked for the 60-69-yr. age group and then declined sharply; for women, frequency rose steadily to a peak at 70 or more yr. It is concluded that an inverse relationship exists between calcium level and frequency of stomach carcinoma. It is suggested that X-irradiation and resultant chromosome breakage (leading to mutations, development of leukemia, etc.) are associated with insufficient calcium levels, especially those of the child in utero. In contrast, the aging process, with its increased calcium levels in the tissues, tends to cause an "immunity" to cancer.

- 70-2111 LACK OF COMMUNICATION BETWEEN CANCEROUS EPITHELIAL CELLS IN TISSUE CULTURE. (E.) Higashino, S. (Columbia U. Coll. Physicians Surg., New York, N. Y.), C. Borek and W. R. Loewenstein. Fed. Proc. 28(2):684, 1969.

- 70-2112 CELLULAR TRANSMISSION OF CANINE LYMPHOMA AND LEUKEMIA IN BEAGLES. (E.) Cohen, H. (U. Kansas Med. Sch., Kansas City), A. L. Chapman, J. Ebert, W. Bopp and C. Gravelle. Fed. Proc. 28(2):750, 1969.

- 70-2113 EPITHELIAL-MESENCHYMAL INTERACTIONS ASSOCIATED WITH MALIGNANT TRANSFORMATION. (E.) Koprowska, I. (Hahnemann Med. Coll. Hosp., Philadelphia, Pa.) and H.-Y. Park. Fed. Proc. 28(2):750, 1969.

- 70-2114 CHROMOSOME STUDIES OF HUMAN LYMPHOCYTOID CELL LINES. (E.) Huang, C. C. (Roswell Park Mem. Inst., Buffalo, N. Y.), T. Imamura and G. E. Moore. Fed. Proc. 28(2): 804, 1969.

See also abstract nos: 1757

AUTHOR INDEX

- Ironson, S. A. 1752
 Jullakhodzhaeva, M. S. 1819
 Jellberg, M. 2053
 Jerca, I. 2020
 Jorian, R. W. 1840
 Jearn, M. J. 1966
 Kawa, S. 2012
 Karia, E. 1982
 Keksandrov, V. A. 1876
 Kexandrov, S. N. 1744
 K-Falluji, M. M. 2058
 Kford, T. C. 2003
 Kgard, F. T. 1833
 Konso, A. 1869
 Kpert, E. 1913
 Ktaner, C. 1963
 Ktshtein, A. D. 2022
 Klachar, E. 1805
 Kndrea, J. 1779
 Kndreoli, A. 1970
 Kndrianov, L. A. 1815
 Knthony, J. J. 1909
 Koshian, H. V. 2060
 Kaki, F. 1756
 Kias, I. M. 1927
 Kmin, K. 2092
 Kshley, D. J. B. 2085,2086
 Ktridge, J. T. 1998
 Kierbach, H. 1753
 Kigl, C. 1959
 Kirelian, L. 2043
 Kva, A. A. 1757
 Ktelrod, D. 2032

 Kba, T. 1874
 Kder, J. P. 1944
 Kilar, J. C. 2094
 Kilenko, N. V. 1793
 Kinnasch, P. 1884
 Krbieri, D. 1734
 Krrrett, C. P. 1981
 Krski, G. 1734
 Krtko, D. 1738
 Krtlett, G. L. 1841
 Krtus, B. 1845
 Ksker, J. F. 1965
 Kther, R. 1956
 Kttifora, H. A. 1849
 Kuer, H. 1952,1954
 Kuer, L. 1916
 Kard, D. 1994
 Kard, J. W. 1994
 Kbawi, G. M. 1890
 Km, J. 1818
 Knedetti, E. L. 1845
 Kntvelzen, P. A. J. 1870
 Knyesh-Melnick, M. 2061
 Kr, A. 1832
 Krcel, N. A. 1910
 Krgger, R. 1733
 Krndt, H. 2080
 Krry, C. L. 2105

 Bielschowsky, M. 1712
 Bierwolf, D. 1735
 Biggs, P. M. 1950
 Bird, C. C. 1807
 Bischoff, F. 1936
 Black, P. H. 2024
 Blankenburg, H. 2090
 Blizzard, R. M. 2106
 Bloom, A. D. 1757
 Blumenson, L. E. 2100
 Blunck, J. M. 1893
 Bock, F. G. 1803
 Bogden, A. E. 1990
 Boisseau, M. 1762
 Bonakdarpour, A. 1875
 Bonmassar, A. 1993
 Bonmassar, E. 1993
 Bopp, W. 2112
 Boquoi, E. 1901
 Borek, C. 2111
 Borisiuk, Iu. P. 1768
 Borneff, J. 1785
 Bosmann, H. B. 2019
 Boutwell, R. K. 1817,1921
 Bowen, J. M. 2014
 Bralow, S. P. 1875
 Braude, V. I. 2073
 Bray, P. F. 2104
 Bricout, F. 2005
 Brière, N. 1885
 Brocco, D. 1786
 Brooks, R. E. 1991
 Bross, I. D. J. 2100
 Brown, E. R. 2052
 Brown, J. M. 1831
 Bruce-Chwatt, L. J. 1960
 Brues, A. M. 1753
 Bryan G. T. 1780,1781,
 1906,1907,1908,1932
 Bryson, G. 1936
 Bulba, A. 1974
 Burns, W. H. 2024
 Burnstein, T. 2006
 Buu-Hoï, N. P. 1861
 Bykovskii, A. F. 2022
 Byrd, B. L. 1775

 Cacciari, P. 1725
 Campbell, T. C. 1938
 Cantor, C. R. 1929
 Cantuti, V. 1786
 Caroline, N. L. 1971
 Cartoni, G. P. 1786
 Chabot, J. F. 1994
 Chai, L. S. 2035
 Chandrasekhara, N. 1939
 Chanh, P.-H. 1861
 Chany, C. 1955
 Chapman, A. L. 2112
 Chassagnon, C. 1741
 Chaudhry, A. P. 1814
 Chaudron, J. M. 1726

 Chermann, J. C. 1977
 Chernov, O. V. 1778
 Chiang, T. 2064
 Chihara, G. 1771
 Chin, T. D. Y. 2093
 Chivu, V. 1750
 Chopra, H. C. 1990,2000
 Christodoulides, L. 1777
 Chu, E. H. Y. 1804
 Chung, M. 2036
 Clarke, J. K. 1998,1999
 Clarke, M. A. 1900
 Clasen, R. A. 1849
 Clement, C. 1745
 Clifford, P. 1719,2039
 Clymer, R. 2047
 Coffey, C. B. 1852
 Cohen, H. 2046,2112
 Cohen, S. M. 1906,1907,1908
 Cohn, M. 1988
 Colburn, N. H. 1921
 Commoner, B. 1848
 Conklin, J. W. 1749,1754
 Cordero Funes, J. 2108
 Cox, B. 1933
 Craddock, V. M. 1872
 Cralley, L. J. 1764
 Crawford, A. M. 1807
 Creaven, P. J. 1797
 Crocker, T. T. 1795
 Currie, A. R. 1807

 Damel, A. 2108
 D'Angostino, F. 2096
 Daniel, M. D. 2040,2041,2042
 Daoust, R. 1885
 Dauty, A. 1762
 Davis, H. J. 2043
 De Angelis, L. 2072
 De Azavedo e Silva, E. 1922
 DeBaun, J. R. 1854
 Defendi, V. 1978
 Delescluse, C. 1732
 Demissie, A. 2039
 Den Engelse, L. 1870
 Deodhar, S. D. 2064
 DeOme, K. B. 1837
 Dermott, E. 1999
 DeRoche, G. M. 1753
 Desbordes, J. 1762
 Deshpande, V. A. 2066
 Dietz, W. 1878
 Dikow, A. 1928
 Dilenno, J. 1714
 Di Marco, A. T. 1891
 DiPaolo, J. A. 1859
 Dixon, F. J. 2063
 Dixon, J. R. 1764
 Dmochowski, L. 1984,2014
 Dobrescu, G. 1745
 Dodd, M. C. 2058
 Dodonova, N. N. 2022

- Doerfler, W. 2059
 Dohan, C., Jr. 2033
 Doljanski, F. 1942
 Dontenwill, W. 1799
 Doré, J. F. 1982
 dos Santos Pinto, D. 1739
 Doto, I. L. 2093
 Doty, S. B. 1981
 Doussset, G. 1762
 Downs, W. G. 2049
 Drago, G. 2072
 Drash, A. 2106
 Dubbs, D. R. 2030
 Dulac, G. C. 2006
 Dungworth, D. L. 1964
 Dupin-Girod, S. 1769
 Dyer, H. M. 1902
- Ebert, J. 2112
 Ebner, H. 1901
 Eckert, L. 1835
 Eckner, R. J. 1975
 Eisenberg, H. 2094
 Elkeles, A. 2110
 Elzay, R. P. 1802
 Emmelot, P. 1870
 Endo, H. 1862
 Epstein, S. M. 1845
 Epstein, S. S. 1779
 Epstein, W. L. 1996
 Erikson, E. 2054
 Erikson, R. L. 2054
 Ernoult, J.-L. 1762
 Ershova, K. P. 1827
 Ertürk, E. 1780, 1906, 1907, 1908
- Fabiani, A. 1880, 1881
 Fahmy, M. J. 1760
 Fahmy, O. G. 1760
 Farber, E. 1845
 Fechner, R. E. 1806
 Fey, F. 1985
 Figge, F. H. J. 1981
 Finzi, C. 1801, 1891, 1892
 Fish, F. 1765
 Flaks, A. 1897
 Flaks, B. 1897
 Fleissner, E. 1728
 Flickinger, J. T. 1972
 Floyd, R. 2061
 Flynt, J. W. 2093
 Fogel, M. 2010
 Fong, C. K. Y. 2002
 Fournaud, S. 1769
 Franceschi, C. 1801, 1892
 Frank, H. 1952
 Franke, R. 1783
 Fraser, C. E. O. 2040, 2041, 2042
 Frei, J. V. 1935
 Fried, M. 2009
 Friedman, M. P. 2056
 Fritsch, S. 1989
 Fukuoka, F. 1771
- Fukuyama, K. 1996
 Fujii, K. 1779
 Fujimura, S. 1874
 Fujinaga, S. 1984
- Gahlen, W. 1717
 Gallmeier, W. M. 2037
 Gallo, R. C. 1968
 Gangadharan, P. 2067
 García, F. G. 2040, 2041, 2042
 Garrafa, V. 1739
 Gates, O. 1758
 Gay, F. W. 1999
 Gelboin, H. V. 1828
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 Vietti, T. J. 2107
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 Zimel, H. 1750
 Ziter, F. A. 2104
 Zülch, K. J. 1736
 zur Hausen, H. 2034, 2057

ABNORMALITIES, CONGENITAL

- association with embryonic tumors, children: 2105
- chromosomal, leukemia epidemiology, review: 1733
- dermatoglyphic, retinoblastoma: 2108
- epidemiology, leukemia clustering, Wisconsin (Green Bay), children: 2093
- pseudohermaphroditism, hypertension and renal degeneration, with Wilms' tumor, children (2 cases): 2106

ABNORMALITIES, DRUG-INDUCED (See Teratogenesis)

ABSORPTION

- skin, dimethylbenzanthracene, mouse: 1815

ACENAPHTHENE, 5-AMINO-

- leukemia/lymphoma (rat) or bladder tumors (mouse): 1772

ACENAPHTHENE, 5-NITRO-

- leukemia/lymphoma or mammary and bladder tumors, mouse: 1772

ACETAMIDE, ALLYLISOPROPYL-

- effect on serum hemopexin, rabbit: 1903

ACETAMIDE, THIO-

- effect on hormone-induced enzymes, animal: 1933

ACRIDAN, 9,9-DIMETHYL-10-DIMETHYLAMINOPROPYL-, HYDROGEN TARTRATE

- toxicity, mouse: 1840

ACTINOMYCIN D (See under Antitumor agents)

ADRENAL NEOPLASMS

- high-occurrence strain of Syrian hamsters: 2097
- induction, oral contraceptive, rat: 1830

ADRENALECTOMY (See under Endocrine ablation)

AFLATOXIN(S)

- analysis
 - animal feeds, methods: 1918
 - chromatography, method: 1917
- teratogenesis, animal: 1859
- liver toxicity
 - human: 1914
 - monkey: 1913
 - mouse: 1915

AFLATOXIN B₁

- DNA complex, properties: 1919
- effect on
 - ameba: 1916
 - DNA-dependent RNA polymerase, rat liver: 1920, 1937
 - synthetic, effect on rat liver: 1937
- toxicity and tumor induction, rat or mouse liver: 1938

AGE FACTORS

- cancer epidemiology, Italy (Milan): 2096
- growth curves, osteosarcoma development: 2089
- tracheobronchial gland development, conventional and germ-free mice: 2102

AIR POLLUTION

- benzpyrene
 - analysis, methods: 1789, 1790
 - bioassay method (mouse): 1791
- polynuclear hydrocarbons, dust, analysis, method: 1786
- radioactive, dosimetry, method: 1753

ALCOHOL CONSUMPTION

- esophagus cancer, geographical distribution, France: 2081

ALKYLATING AGENTS (See under Antitumor agents)

AMINES, AROMATIC

- occupational exposure, bladder cancer: 1782

ANDROGENS

- metabolism, women with larynx cancer: 1835

ANTHRANILIC ACID, 3-HYDROXY-

- bladder tumors, effect of ascorbic acid, mouse: 1931

ANTIBIOTICS

- chromosomal abnormalities, review: 1716

ANTICONVULSANTS

- hydantoin type, lymphoma, human: 1909, 1910

ANTIDEPRESSANTS

- toxicity, mouse: 1840

ANTILYMPHOCYTE SERUM (See under Immune serum)

ANTITUMOR AGENTS

- actinomycin D
 - effect on polyoma-infected cells: 2014
- cyclophosphamide
 - stimulation of brain tumor, human: 1747
 - toxicity, liver, mechanism, rat: 1860
- cytosine arabinoside
 - effect on DNA, sarcoma virus-infected or -transformed mouse cells: 1956, 1958
- mitomycin C
 - effect on SV40- or polyoma virus-transformed cells: 2010, 2024
- polyfunctional alkylating agents
 - teratogenesis, animal: 1859
- vinblastine
 - effect on dimethylbenzanthracene cheek pouch tumor, hamster: 1813

ARSENIC

- skin cancer, human: 1776

ASBESTOS

- biological effects, review: 1713
- occupational exposure
 - bronchial cancer: 1762
 - cancer incidence, New York and New Jersey, review: 2071
 - leukemia/lymphoma, New York: 1763
- trace metals, effect on benzpyrene hydroxylase, mouse lung: 1764

ATHEROSCLEROSIS, CALCIFIED

- association with stomach cancer and ulcer: 2110

AUTOIMMUNE DISEASES (See under Immunity disorders)

AZAPROPAZONE (See 1,2,4-Benzotriazine, 3-dimethyl-amino-7-methyl-1,2-(n-propylmalonyl)-1,2-dihydro-)

AZOBENZENE, 2,5-DIMETHOXY-4-AMINO-

- toxicity, rat: 1889

AZOBENZENE, 4-DIMETHYLAMINO-

- derivatives, structure-activity relationship, rat: 1890

- liver tumors, rat: 1885, 1886, 1940

- and N⁴-oxide, toxicity, mechanism, liver, rat: 1860

AZOBENZENE, 2-METHYL-4-DIMETHYLAMINO-

- liver tumors, rat: 1887

AZOBENZENE, 3'-METHYL-4-DIMETHYLAMINO-

- binding, mechanism, rat liver proteins: 1777

- BENZENE, 3-METHYL-4-DIMETHYLAMINO- (Contd.)
 liver tumors, rat: 1847, 1887, 1888, 1891, 1893
 BENZENE, 3-METHOXY-4-AMINO-
 liver tumors, rat: 1889
 TOLUENE, o-AMINO-
 liver tumors, mouse: 1895
- CACTERIOPHAGE
 mutagenesis, nitroquinoline oxide: 1862
 NZ(c)ACRIDINE, 7,10-DIMETHYL-
 effect on crustacean eggs: 1861
 2-BENZANTHRACENE
 analysis, petrochemical effluents, method:
 1827
 effect on microsomal enzymes, mechanism, hamster
 cells: 1828
 photodynamic effect, Neurospora or hamster
 cells: 1804
 BENZANTHRACENE
 skin tumors, mouse: 1784
 NZANTHRACENE, 1:2,5:6-DI-
 photodynamic effect, Neurospora or hamster
 cells: 1804
 skin tumors, mouse: 1784
 NZANTHRACENE, 7,12-DIMETHYL-
 absorption, skin, mouse: 1815
 brain tumors, rat: 1819
 cheek pouch dyskeratosis, effect of laser ir-
 radiation, hamster: 1926
 effect on
 cutaneous nerves, mouse or rabbit: 1818
 virus-free preneoplastic mammary outgrowths,
 mouse: 1836
 kidney tumors, rat, effect of oophorectomy:
 1820
 leukemia (mouse): 1808, 1809, 1810
 associated mammary tumor, effect of oopho-
 rectomy: 1811
 mammary tumors (rat): 1821, 1823, 1824, 1825,
 1898
 virus-like particles: 2000
 nucleic acid and protein binding, rat tissues
 or tumor cells: 1801, 1805
 photodynamic effect, Neurospora or hamster
 cells: 1804
 s.c. sarcoma, hamster: 1816
 salivary gland tumors, rat: 1812, 1814
 skin tumors, mouse: 1784, 1803, 1815, 1817
 teratogenesis, rat: 1807
 uptake and clearance, mammary gland, rat: 1826
 NZANTHRACENE, 7-HYDROXYMETHYL-
 teratogenesis, rat: 1807
 NZANTHRACENE, 7-HYDROXYMETHYL-12-METHYL-
 teratogenesis, rat: 1807
 NZANTHRACENE, 12-HYDROXYMETHYL-7-METHYL-
 teratogenesis, rat: 1807
 NZANTHRACENE, 7,8,12-TRIMETHYL-
 leukemia and mammary tumors, rat: 1829
 3'-BENZIDINEDICARBOXYLIC ACID
 leukemia and lung or liver tumors, rat: 1923
 ZO(g,h,i)PERYLENE
 skin tumors, mouse: 1784
 2,4-BENZOTRIAZINE, 3-DIMETHYLAMINO-7-METHYL-
 1,2-(n-PROPYLMALONYL)-
 toxicity, mouse: 1840
- 1,2-BENZPERYLENE
 analysis, coffee substitutes: 1800
 2-BENZPYRENE
 photodynamic effect, Neurospora or hamster
 cells: 1804
 3,4-BENZPYRENE
 air pollution
 analysis, methods: 1789, 1790
 bioassay method (mouse): 1791
 analysis
 coffee substitutes: 1800
 soil and plants, USSR: 1787, 1792
 diagnostic use, ruptured placental membranes,
 human: 1798
 dietary, stomach cancer, Iceland: 2083
 distribution
 human: 1796
 skin, mouse: 1794
 effect on microsomal metabolism, rat Liver:
 1797
 hydroxylase
 effect of trace metals and asbestos, mouse
 lung: 1764
 methylcholanthrene induction, rat liver or
 hepatoma: 1904
 lung tumors, rat, pathology: 1793
 metabolism and distribution, rat or hamster,
 effect of vehicle: 1799
 photodynamic effect, Neurospora or hamster
 cells: 1804
 squamous metaplasia of trachea, effect of citral
 or vitamin A in vitro, hamster: 1795
 tobacco smoke component, lung tumors, mouse:
 1768
 tumor regression by adenovirus 12-infected or
 transformed cells, hamster: 1925
 water pollution, method of removal: 1788
 BETEL
 chewing, esophagus cancer, Ceylon: 2081
 4-BIPHENYLACETAMIDE, 4'-FLUORO-
 kidney tumors, growth rate, rat: 1858
 BLADDER
 effect of diphenylhydantoin, rat: 1912
 BLADDER CARCINOGENESIS
 bracken fern fractions, mouse: 1781
 detergent additives (acenaphthenes), mouse:
 1772
 4-diphenylamine, rabbit: 1850
 fluorenylacetamide, rabbit: 1850
 hydroxyanthranilic acid, effect of ascorbic
 acid, mouse: 1931
 N-(4-[5-nitro-2-furyl]-2-thiazolyl)formamide,
 mouse: 1908
 β-naphthylamine, rabbit: 1850
 occupational exposure to aromatic amines: 1782
 saccharin, mouse: 1780
 tobacco, review: 1714, 1715
 BONE
 gallium distribution, leukemic or nonleukemic
 AKR/J mice: 1775
 leukemia virus particles, high-leukemia mouse
 strains (AKR and C3H/Fg): 1981
 BONE NEOPLASMS
 epidemiology
 dogs, USSR (Moscow): 2098
 East Germany: 2090

BONE NEOPLASMS (Contd.)

osteosarcoma, age factors, skeletal growth rate: 2089

BRACKEN FERN (See Pteris aquilina)

BRAIN

acute cerebellar encephalopathy, association with neuroblastoma, cases and review: 2104
effect of methylnitrosourea, fetal rat: 1876, 1879

BRAIN NEOPLASMS (See also Nervous system neoplasms)

induction
animal, review: 1736
dimethylbenzanthracene, rat: 1819
fluorenylacetaamide, effect of lead sub-acetate, rat: 1849
methylnitrosourea, rabbit: 1877, 1878
rat: 1876, 1877, 1880, 1881
injury, child: 1738
stimulation, radiotherapy or antitumor agent, human: 1747

BREAST NEOPLASMS (See Mammary neoplasms, human)

Cannabis CONSTITUENTS

analysis
cigarette smoke: 1765
mouth and fingers of marihuana smokers: 1766

CANTHARIDIN

skin tumor promotion, mechanism, mouse: 1817

CARBAMIC ACID COMPOUNDS (See also Urethan)

zinc-dithiocarbamic acid type herbicides, lung tumors, mouse: 1778

CARBON TETRACHLORIDE

toxicity, liver, mechanism, rat: 1860

CARCINOGENESIS, CHEMICAL

brain, animal, review: 1736
mouse cervix, epithelial-mesenchymal interactions: 2113

CARCINOGENS CHEMICAL

chronic toxicity tests, animal, methods: 1759
detection of weakly active carcinogens, method: 1771
mutagenesis, mechanism, Drosophila: 1760

CELL GROWTH KINETICS

breast cancer, mathematical model: 2100
dimethylbenzanthracene-induced mammary tumors, rat: 1824, 1825
fluorobiphenylacetamide kidney tumors, rat: 1858

Harvey sarcoma virus-transformed rat cells: 1961

normal or leukemic human cell lines: 2099
spontaneous malignant transformation, rat fibroblast cultures: 2101
theoretical model, mouse sarcomas: 2050

CELL SURFACE PROPERTIES

cell-to-cell contact in vitro, epithelial tumor cells: 2111

CERVIX UTERI NEOPLASMS

early invasive form, chromosomes, review: 1722
epidemiology, review: 1721
herpesvirus Type 2 (genital) antibodies: 2043
induction
epithelial-mesenchymal interactions, mouse: 2113

CERVIX UTERI NEOPLASMS (Contd.)

induction (Contd.)
plastics, mouse: 1836
injuries, human: 1737
radiotherapy-induced reticulum cell sarcoma: 1745

CHEEK POUCH NEOPLASMS

dimethylbenzanthracene-induced (hamster) effect of
alcohol or cigarette smoke: 1802
laser irradiation: 1926
vinblastine on metastases: 1813

CHLORAMPHENICOL

effect on
diethylnitrosamine liver tumors, rat: 1869
methylidimethylaminoazobenzene liver tumors, rat: 1893

4-CHOLESTEN-3-ONE, 6 β -HYDROXY-

s.c. tumors, mouse: 1936

CHROMOSOMES

aberrations, atomic radiation exposure, Japan: 1757
cervix cancer, review: 1722
congenital anomalies, leukemia, human, review: 1733
DNA virus-induced tumors, review: 1732
effect of
carcinogens, review: 1716
nitroquinoline oxide, rat tumor cells: 1864
Gross leukemia virus-transformed rat thymus cells: 2065
human leukemia and lymphoma cell lines, cloning efficiency: 2114
nitroquinoline oxide-transformed hamster embryo cells: 1863
spontaneous or induced viral leukemia, mouse, review: 1734, 1735

CIGARETTE SMOKING (See Tobacco smoking)

CITRAL (See 2,6-Octadienal, 3,7-dimethyl-)

CLUSTERING (See under Disease outbreaks)

COCARCINOGENS, CHEMICAL

cell culture test: 1761

COLON

familial polyposis, malignant transformation, enzyme histochemistry: 2103

COLON NEOPLASMS

epidemiology, single- or multiple-"hit" model: 2085, 2086

CONNECTIVE TISSUE

⁸⁵Sr or ⁹⁰Sr retention, dosimetry, dog: 1753

CONNECTIVE TISSUE NEOPLASMS

epidemiology, East Germany: 2090
mesothelioma, induction, MC29 (avian leukosis) virus-infected cells, chicken: 1994
uterine leiomyosarcoma, androgen + estrogen-induced, hamster: 1833

CONTRACEPTIVES, ORAL

fibroadenoma of breast, human: 1806, 1831
multiple tumor types, rat: 1830

CORPUS UTERI NEOPLASMS

epidemiology, Ohio (Lucas County), review: 207
induction
methylcholanthrene, hormone effects, mouse: 1901
oral contraceptive, rat: 1830
plastics, mouse: 1836

CORPUS UTERI NEOPLASMS (Contd.)
 leiomyosarcoma, induction, androgen + estrogen,
 hamster: 1833
 ORTISONE ACETATE
 enhancement of dimethylbenzanthracene leukemo-
 genesis, mouse: 1810
 ROTON OIL
 skin tumor promotion, mechanism, mouse: 1817
 ROTON OIL PHORBOL ESTERS
 cell culture test: 1761
 cocarcinogenesis, skin, mouse: 1784
 YCASIN
 kidney tumors, rat: 1774
 YCASIN AGLYCONES
 toxicity, mouse or rat: 1924
 CLOPHOSPHAMIDE (See under Antitumor agents)
 TERGENT ADDITIVES
 acenaphthenes, metabolism (dog) or carcinogenic
 effects (mouse and rat): 1772
 ETARY FACTORS (See also under Foods)
 mycotoxins, liver cancer, Ethiopia: 2084
 stomach cancer epidemiology, Iceland: 2083
 ETHYLSTILBESTROL
 effect on DMBA mammary tumors, rat: 1822
 mammary carcinogenesis
 human, male: 1834
 virus-like particles, rat: 2000
 ETHYLSTILBESTROL + TESTOSTERONE PROPIONATE
 implantation, uterine leiomyosarcoma, hamster:
 1833
 METHACRINE (See Acridan, 9,9-dimethyl-10-
 dimethylaminopropyl-, hydrogen tartrate)
 DIPHENYLAMINE
 bladder tumors, rabbit: 1850
 PHENYLMETHANE, 4,4'-DIAMINO-
 toxicity, rat: 1894
 PHENYLMETHANE, 3,3'-DICHLORO-4,4'-DIAMINO-
 liver and lung tumors, rat: 1894
 SEASE OUTBREAKS
 leukemia clusters
 children, Wisconsin (Green Bay): 2093
 time between case pairs, Connecticut: 2094
 virus diseases and radiation exposure, Japan:
 2095
 reticulum cell sarcoma, leukosis- and lymphoma-
 free colony of Japanese quail, Hawaii
 (Honolulu): 2051
 SEASE TRANSMISSION
 cellular, leukemia or lymphoma, dog: 2112
 serum antibodies to leukemic antigens, leukemia
 pts. and their relatives: 1969
 STRIBUTION
 benzpyrene
 effect of vehicle, rat or hamster: 1799
 human: 1796
 skin, mouse: 1794
 dimethylbenzanthracene
 DNA binding, rat: 1801
 mammary gland, rat: 1826
 gallium, leukemic or nonleukemic AKR/J mice:
 1775
 ST
 atmospheric
 benzpyrene-containing, stomach tumors, mouse:
 1791

DUST (Contd.)
 atmospheric (Contd.)
 polynuclear hydrocarbons, analysis, method:
 1786
 ELECTRICITY
 current, tumor stimulation, rat: 1750
 EMBRYO (See also Teratogenesis)
 brain, effect of methylnitrosourea, rat: 1876,
 1879
 crustacean, effect of carcinogens: 1861
 ENDOCRINE ABLATION
 adrenalectomy
 effect on fluorenylacetamide liver tumors,
 mouse: 1843
 oophorectomy, effect on dimethylbenzanthracene
 tumor induction, mouse or rat: 1811, 1820,
 1822, 1824
 ENVIRONMENTAL FACTORS
 altitude, effect on radiation carcinogenesis,
 mouse: 1749
 lymphoma, Saudi Arabia (Dhahran): 2091
 nasopharynx cancer, Chinese and other Oriental
 populations, review: 1719
 ENZYMES
 aldolase and glucose-6-phosphatase, diethyl-
 nitrosamine hepatoma, rat: 1928
 atypical, familial polyposis of colon with
 malignant transformation: 2103
 benzpyrene hydroxylase
 effect of trace metals and asbestos, mouse
 lung: 1764
 methylcholanthrene induction, rat liver or
 hepatoma: 1904
 collagen:galactosyl transferase, SV40- or
 polyoma-transformed cells: 2019
 endonuclease, polyoma-transformed hamster cells:
 2060
 fluorenylacetamide liver tumor, rat: 1846
 β-glucuronyltransferase, induced or transplanted
 hepatoma, rat: 1902
 microsomal
 benzanthracene induction, mechanism, hamster
 cells: 1828
 methylcholanthrene induction, mechanism,
 rabbit: 1903
 relationship to growth rate, dimethylbenzanthra-
 cene mammary tumors, rat: 1825
 tryptophan oxygenase, hormone induction, effect
 of thioacetamide, animal: 1933
 EPIDEMIOLOGY
 all tumors
 age factors, Italy (Milan): 2096
 Armenian SSR (Chuvash): 2069
 India (Bombay), ethnic groups: 2066, 2067
 kidney transplantation with immunosuppression:
 2087
 occupational asbestos exposure, New York and
 New Jersey, review: 2071
 radiation exposure: 1755
 smoking: 2070, 2071
 socioeconomic status: 2070
 South Africa (Johannesburg), ethnic groups:
 2068
 trace metals in drinking water, Italy
 (Pesaro): 2072

EPIDEMIOLOGY (Contd.)

- benign fibroadenoma of breast, oral contraceptives, Texas (Houston): 1806
- bone tumors
 - age factors, skeletal growth rate: 2089
 - East Germany: 2090
- breast cancer
 - hormone metabolism, review: 1724, 1725
 - lactation and reproductive histories, Greece (Athens): 2079
 - premenopausal and postmenopausal patterns, Germany (Berlin): 2080
 - review: 1723
- cervix cancer, review: 1721
- chromosomal aberrations, atomic radiation exposure, Japan: 1757
- colon/rectum cancer, single- or multiple-"hit" models: 2085, 2086
- connective tissue tumors, East Germany: 2090
- esophagus cancer
 - Ceylon, betel chewing: 2081
 - France, alcohol consumption, geographical distribution: 2081
 - South Africa (Johannesburg), ethnic groups: 2068
- extrapulmonary tumors, TB, USSR (Moscow): 2073
- familial multiple tumor types including neuroblastoma: 2088
- female genital cancer, USSR (Kirovabad), ethnic groups: 2078
- herpesvirus Type 2 (genital) antibodies, cervix cancer: 2043
- Hodgkin's disease, worldwide, review: 1726
- leukemia
 - asbestosis, New York: 1763
 - bovine leukosis areas, Poland (Zlatow district): 1967
 - congenital chromosomal anomalies, review: 1733
 - Connecticut, clustering: 2094
 - Japan, clustering: 2095
 - Wisconsin (Green Bay), children, congenital defects, clustering: 2093
- liver tumors, Ethiopia (Addis Ababa), dietary factors and folk medicines: 2084
- lung cancer
 - TB, treatment (pneumothorax), radiation and smoking: 1748
 - USSR (Moscow): 2073
- lymphoma
 - asbestosis, New York: 1763
 - bovine leukosis areas, Poland (Zlatow district): 1967
 - hydantoin anticonvulsants, Ohio (Cincinnati): 1909
 - Iran: 2092
 - Saudi Arabia (Dhahran), environmental factors: 2091
- malignant melanoma, Switzerland: 2076
- nasopharynx cancer
 - Chinese, California: 2075
 - review: 1719
 - Japan and Taiwan: 2038
- serum Epstein-Barr virus antibodies
 - cancer pts., Japan and Taiwan: 2038
 - West Germany (Essen): 2037

EPIDEMIOLOGY (Contd.)

- stomach cancer
 - air pollution, bioassay method: 1791
 - Iceland, dietary factors: 2083
- thyroid cancer, Hawaii (Oahu): 2074
- uterus cancer, Ohio (Lucas County), review: 2071
- EPIDEMIOLOGY, VETERINARY
 - adrenal tumors, high-tumor strain of Syrian hamsters: 2097
 - all tumors, dogs, USSR (Moscow): 2098
 - bovine leukosis, association with human leukemia/lymphoma, Poland (Zlatow district): 1967
 - reticulum cell sarcoma, leukosis- and lymphoma-free colony of Japanese quail, Hawaii (Honolulu): 2051
- EPOXY COMPOUNDS
 - effect on crustacean eggs: 1861
- ESOPHAGUS NEOPLASMS
 - chemical burn stenosis: 1741
 - epidemiology
 - Ceylon, betel chewing: 2081
 - France, alcohol consumption, geographical distribution: 2081
 - South Africa (Johannesburg), ethnic groups: 2068
- ESTRADIOL
 - effect on dimethylbenzanthracene mammary tumors, rat: 1821, 1824
- ESTROGENS
 - metabolism, women with larynx cancer: 1835
 - mixed (Premarin), enhancement of adenovirus-12 or spontaneous transformation, hamster cells: 2002
 - urinary, breast cancer etiology, review: 1724
- ETHANOL
 - tumor promotion, hamster cheek pouch: 1802
- ETHIONINE
 - effect on crustacean eggs: 1861
 - liver tumors, effect of orotic acid, rat: 1847
- ETHNIC GROUPS
 - breast cancer, review: 1723
 - cancer epidemiology
 - India (Bombay), Hindus and Parsis: 2066, 2067
 - South Africa (Johannesburg): 2068
 - cervix cancer, review: 1721
 - female genital cancer, USSR (Kirovabad): 2078
 - nasopharynx cancer
 - Chinese, California: 2075
 - review: 1719
- EYE NEOPLASMS
 - retinoblastoma, dermatoglyphic abnormalities: 2108
- FATS
 - heated or unheated, effect on methylcholanthrene g.i. tumors, guinea pig: 1899
- FATTY ACIDS
 - deficiency, effect on fluorenylacetamide liver tumors, rat: 1844
- FEED ANIMAL
 - aflatoxin content, detection method: 1918

- JORANTHENE
 analysis, coffee substitutes: 1800
 2-FLUORENYLACETAMIDE
 bladder tumors, rabbit: 1850
 brain tumors, effect of lead, rat: 1849
 effect on properties of oligonucleotides: 1929
 liver tumors
 mouse: 1843
 rat: 1842, 1844, 1845, 1846, 1847, 1848, 1852, 1939
 2,7-FLUORENYLDIACETAMIDE
 liver tumors, effect of reserpine, sex factors, mouse: 1856
 2-FLUORENYLACETAMIDE, N-HYDROXY-
 binding to protein, rat liver: 1852, 1853, 1854, 1855
 liver tumors, mechanism, rat: 1852, 1853, 1854, 1855
 2,7-FLUORENYLENEBISACETAMIDE
 liver and intestinal tumors, rat: 1857
 ADDITIVES
 liver or lung tumors and lymphoma, mouse: 1779
 DIETARY FACTORS (See also Dietary factors)
 benzpyrene content, stomach cancer, Iceland: 2083
 coffee substitutes, carcinogen content: 1800
 saccharin, bladder tumors, mouse: 1780
 PROCESSING METHODS
 smoking of meat or fish, stomach cancer, Iceland: 2083
 AMIDE, N-(4-[5-NITRO-2-FURYL]-2-THIAZOLYL)-
 bladder tumors, mouse: 1908
 MIC ACID 2-(4-[5-NITRO-2-FURYL]-2-THIAZOLYL)-
 HYDRAZIDE
 leukemia and solid tumors, mouse: 1907
 LIUM
 distribution, leukemic or nonleukemic AKR/J mice: 1775
 TROINTESTINAL CARCINOGENESIS
 benzpyrene-containing atmospheric dust, mouse: 1791
 colon/rectum cancer, single- or multiple-"hit" theory: 2085, 2086
 dimethylhydrazine, hamster: 1905
 fluorenylacetamide, effect of sunflower oil, rat: 1842
 fluorenylenebisacetamide, rat: 1857
 formic acid 2-(4-[5-nitro-2-furyl]-2-thiazolyl)-hydrazide, mouse: 1907
 methylcholanthrene, effect of heated or unheated fats, guinea pig: 1899
 methylnitrosourea, transplacental, rat: 1876
 N-methyl-N'-nitro-N-nitrosoguanidine, rat: 1873, 1874, 1875
 oral contraceptive, rat: 1830
 pesticides, occupational, case and review: 1720
 TROINTESTINAL NEOPLASMS
 epidemiology, trace metal content of drinking water, Italy (Pesaro): 2072
 GENETICS, ANIMAL
 development of high- and low-cancer NZB mouse strains, review: 1712
 high-adrenal tumor strain of Syrian hamsters: 2097
 GENETICS, ANIMAL (Contd.)
 MH2 reticuloendothelioma virus resistance, chickens: 1950
 mammary tumors
 dogs, USSR (Moscow): 2098
 transplantability, virus-positive or -negative mice: 1997
 strain differences
 AKR leukemia virus susceptibility, mouse: 1983
 dimethylbenzanthracene leukemogenesis, mouse: 1808
 GENETICS, HUMAN
 chromosomal anomalies, leukemia incidence, review: 1733
 familial melanoma (3 generations): 2077
 hereditary skin diseases, malignant transformation: 1742
 melanoma, review: 1718
 neuroblastoma: 2088
 susceptibility to chemical leukemogenesis: 1910, 1911
 GENETICS, MICROBIAL
 tumor viruses, review: 1729
 GENETICS, POPULATION
 nasopharynx cancer, Chinese and other Oriental populations, review: 1719
 GENITAL NEOPLASMS
 venereal sarcomas, epidemiology, dogs, USSR (Moscow): 2098
 GENITAL NEOPLASMS, FEMALE
 epidemiology
 India (Bombay), Hindus and Parsis: 2066, 2067
 USSR (Kirovabad), ethnic groups: 2078
 GERM-FREE STATUS
 age-related tracheobronchial gland development, mouse: 2102
 Rous sarcoma virus-induced leukemoid reaction, rat: 1953
 GLUCURONIDES
 metabolism, effect of diethylnitrosamine, animal: 1927
 HEART NEOPLASMS
 induction, dimethylurea + nitrite, rat: 1882
 HEMATOPOIESIS
 erythropoietin-stimulating factor, effect of dimethylnitrosamine, monkey or dog: 1871
 HEMOPEXIN
 serum, effect of methylcholanthrene, rabbit: 1903
 HERBICIDES (See also Pesticides)
 occupational exposure, stomach cancer, case and review: 1720
 zinc-dithiocarbamic acid type, lung tumors, mouse: 1778
 HISTONES
 synthesis, polyoma- or SV40-infected cells: 2018
 HORMONES
 dependence, androgen + estrogen-induced uterine leiomyosarcoma, hamster: 1833
 metabolism, breast cancer, review: 1724, 1725
 pre- and postmenopausal breast cancer
 epidemiology, Germany (Berlin): 2080

HORMONES, CONTRACEPTIVE

- fibroadenoma of breast, human: 1806
- multiple tumor types, rat: 1830

HYDANTOIN COMPOUNDS

- anticonvulsants, lymphoma, human: 1909, 1910

HYDANTOIN, DIPHENYL-

- effect on bladder, rat: 1912

HYDRAZINE, 1,2-DIMETHYL-

- liver and g.i. tumors, hamster: 1905

2-HYDRAZINOTHIAZOLE COMPOUNDS

- structure-activity relationship, rat: 1906

HYDROCARBONS, POLYCYCLIC AROMATIC

- analysis
 - atmospheric dust, method: 1786
 - water supply, method: 1785
- structure-activity relationships: 1783

HYPOTHALAMUS

- estrogen implant, stimulation of DMBA mammary tumor, rat: 1821

IMMUNE SERUM

- antilymphocyte serum, effect on polyoma virus-induced runting and tumor, hamster: 2058
- Friend leukemia virus antiserum, production, mouse, rat or rabbit: 1976

IMMUNITY

cellular

- adenovirus-12 hamster tumors: 2003
- DNA virus-induced tumors, review: 1731
- Epstein-Barr virus-containing cells: 2039
- mouse or rat tumors induced by rat-adapted sarcoma pseudotype (MSV-33) of Rauscher leukemia virus: 1980
- polyoma virus-transformed cells, low-tumor clones, 2011
- spontaneous mammary tumors, MTV-free mice: 2053
- SV40
 - induced hamster tumor: 2021
 - transformed cells: 2027, 2062

host

- dimethylbenzanthracene leukemia, mouse: 1809
- effect of Friend leukemia virus, mouse: 1972, 2064
- Gross viral leukemia cells, non-leukemic AKR mouse: 1982
- L-1210 leukemia-bearing mouse: 1993
- MTV-free mice with spontaneous mammary tumors: 2053
- polyoma tumor-bearing mouse or hamster: 2013, 2015
- serum antibodies to leukemic antigens, leukemia pts. and their relatives: 1969
- SV40 tumor-bearing hamster: 2023
- virus-induced myeloid leukemia, mouse: 1987
- precipitation reaction between tobacco extracts and human sera: 1769

IMMUNITY DISORDERS

- autoimmunity, effect of polyoma or Rauscher viruses, NZB mice: 2048, 2063
- congenital hypogammaglobulinemia with Hodgkin's disease, case (child) and review: 2107
- polyoma virus-induced runting, effect of anti-lymphocyte serum, hamster: 2058

IMMUNOSUPPRESSION

- Friend leukemia virus, normal or tumor-bearing mouse: 1972, 2064
- kidney transplantation, induction of RES tumors: 2087
- malaria, effect on Harvey viral sarcoma, mouse: 1960
- INJURIES (See also under Scar tissue and Stress)
 - brain, malignant transformation, child: 1738
 - burns, malignant transformation, skin cancer incidence: 1740
 - cervix cancer, human: 1737
 - chemical burn stenosis, cancer of esophagus: 1741
 - dental prosthesis, hard palate tumors: 1739
 - electrical, tumor stimulation, rat: 1750
 - radiation dermatitis, skin cancer: 1740, 1743

INSECTS

- Drosophila*, carcinogen-induced mutations: 1760

ISOPROTERENOL

- effect on DNA, rat salivary gland: 1930

INTERFERON

- effect on Moloney sarcoma virus-transformed mouse cells: 1955

INTESTINE, LARGE, NEOPLASMS

induction

- fluorenylenebisacetamide, rat: 1857

INTESTINE, SMALL, NEOPLASMS

induction

- fluorenylenebisacetamide, rat: 1857

KIDNEY

- dimethylbenzanthracene binding, DNA, rat: 1801
- β -naphthylamine binding, DNA, RNA and protein, mouse: 1851
- toxicity, dimethylnitrosamine, monkey or dog: 1871

KIDNEY CARCINOGENESIS

- cycasin, rat: 1774
- dimethylbenzanthracene, rat, effect of oophorectomy: 1820
- dimethylurea + nitrite, rat: 1882
- fluorobiphenylacetamide, tumor growth rate, rat: 1858
- methylnitrosourea, transplacental, rat: 1876
- tobacco, review: 1715

KIDNEY NEOPLASMS

- induction, triploid or normal frog larvae: 2045
- Wilms' tumor, associated pseudohermaphroditism, hypertension and renal degeneration, cases: 2106

LACTATION

- history, breast cancer incidence, Greece (Athens): 2079

LARYNX NEOPLASMS

- sex hormone metabolism, women: 1835

LEAD SUBACETATE

- effect on fluorenylacacetamide brain tumors, rat: 1849

LEUKEMIA EXPERIMENTAL (See also Virus, leukemia/lymphoma)

- canine
 - cellular transmission: 2112

LEUKEMIA, EXPERIMENTAL (Contd.)

- canine, (Contd.)
 - cellular transmission (Contd.)
 - tumor pathology, mouse: 2046
- L-1210 (mouse), primary antibody response: 1993
- L5178Y (mouse), cells, effect of arboviruses: 2049
- tissue distribution of gallium, AKR/J mice: 1775

LEUKEMIA, HUMAN

- associated with solid tumors, pathogenesis, cases and review: 1727
- cell lines, properties: 2099, 2114
- epidemiology
 - congenital chromosomal anomalies, review: 1733
- Connecticut, clustering: 2094
- Japan, clustering: 2095
- occupational asbestos exposure, New York: 1763
- Wisconsin (Green Bay), children congenital defects, clustering: 2093
- properties of WBC RNA: 1968, 1970
- serum antibodies to leukemic antigens, pts. and their relatives: 1969
- tissue extract, pathology of induced leukemia, mouse: 2046

LEUKEMOGENESIS, EXPERIMENTAL (See also Radiation leukemogenesis, experimental and Virus, leukemia/lymphoma)

- benzidinedicarboxylic acid, rat: 1923
- detergent additives (acenaphthenes), mouse or rat: 1772
- dimethylbenzanthracene, mouse: 1808, 1809, 1810, 1811
- food additives, lymphoma, mouse: 1779
- formic acid 2-(4-[5-nitro-2-furyl]-2-thiazolyl)-hydrazide, mouse: 1907
- lung or kidney isografts (XVII/G mice), C57BL mice: 1992
- methylnitrosourea
 - mouse: 1935
 - transplacental, rat: 1876
- squirrel herpesvirus, marmoset: 2041, 2042
- trimethylbenzanthracene, rat: 1829
- urethan, virus particles, mouse: 1991

LEUKEMOGENESIS, HUMAN (See also Radiation leukemogenesis, human)

- anticonvulsants of hydantoin type: 1909, 1910
- immunosuppressive therapy for kidney transplants: 2087
- phenylbutazone, genetic factors: 1911
- treated solid tumors, cases and review: 1727

LEUKEMOID REACTION

- Rous sarcoma virus induction, germ-free or conventional rat: 1953

LIPOPROTEINS

- serum, fatty acid-deficient rats with fluorenylacetamide hepatoma: 1844

LIVER

- aflatoxin toxicity
 - human: 1914
 - monkey: 1913
 - mouse: 1915, 1938
 - rat: 1938

LIVER (Contd.)

- benzpyrene hydroxylase, methylcholanthrene induction, rat: 1904
- dimethylnitrosamine toxicity, dog or monkey: 1871
- DNA
 - dependent RNA polymerase, effect of aflatoxin, rat: 1920, 1937
 - dimethylbenzanthracene binding, rat: 1801
 - methylnitro-N-nitrosoguanidine uptake, rat: 1872
 - β -naphthylamine binding, mouse: 1851
- hepatocarcinogen toxicity, mechanism, rat: 1860
- microsomes, effect of benzpyrene, rat: 1797
- portacaval shunt, effect on DMBA mammary tumors, rat: 1823
- proteins
 - azo dye binding, rat: 1777
 - β -naphthylamine binding, mouse: 1851
 - RNA, β -naphthylamine binding, mouse: 1851

LIVER CARCINOGENESIS

- aflatoxin B1, rat or mouse: 1938
- o*-aminoazotoluene, mouse: 1895
- azobenzene compounds, structure-activity relationship, rat: 1890
- benzidinedicarboxylic acid, rat: 1923
- dichlorodiaminodiphenylmethane, rat: 1894
- diethylnitrosamine, rat: 1869, 1928
- dimethylaminoazobenzene, rat: 1885, 1886, 1890, 1940
- dimethylhydrazine, hamster: 1905
- dimethylnitrosamine
 - mouse: 1870
 - trout: 1868
- dinitrosopiperazine, mouse: 1883
- ethionine, effect of orotic acid, rat: 1847
- fluorenylacetamide
 - effect of adrenalectomy, mouse: 1843
 - rat: 1842, 1844, 1845, 1847, 1848, 1852, 1939
- fluorenylenebisacetamide, rat: 1857
- fluorenyldiacetamide, sex factors, effect of reserpine, mouse: 1856
- food additives, mouse: 1779
- hydroxyfluorenylacetamide, rat: 1852, 1853, 1854, 1855
- methoxyaminoazobenzene, rat: 1889
- methylcholanthrene, enzymes, rat: 1902
- methyldimethylaminoazobenzene, rat: 1847, 1887, 1888, 1891
- nitrosomorpholine, rat: 1884
- oral contraceptive, rat: 1830

LIVER NEOPLASMS

- epidemiology, Ethiopia (Addis Ababa), hepatotoxic taenicides and dietary mycotoxins: 2084

LUNG

- benzpyrene hydroxylase, effect of trace metals and asbestos, mouse: 1764
- dimethylbenzanthracene-DNA binding, rat: 1801
- effect of asbestos, review: 1713
- mucociliary efficiency, smokers: 1770
- LUNG CARCINOGENESIS
 - azapropazone, mouse: 1840
 - benzidinedicarboxylic acid, rat: 1923

LUNG CARCINOGENESIS (Contd.)

- benzpyrene, rat: 1793
- dimethacrine, mouse: 1840
- dimethylnitrosamine, mouse: 1870
- dinitrosopiperazine, mouse: 1883
- fluoroscopic radiation and/or therapeutic pneumothorax, TB: 1748
- food additives, mouse: 1779
- formic acid 2-(4-[5-nitro-2-furyl]-2-thiazolyl)-hydrazide, mouse: 1907
- occupational asbestos exposure: 1762
- radiation, mouse: 1749, 1754
- tobacco
 - review: 1714, 1715
 - mouse: 1768
- urethan (mouse): 1778, 1838, 1839, 1840
 - associated virus-containing leukemia: 1991
 - effect of thymectomy and radiation: 1841
- zinc-dithiocarbamic acid herbicides, mouse: 1778

LUNG DISEASES

- tuberculosis
 - lung and other cancer occurrence, USSR (Moscow): 2073
 - therapeutic pneumothorax and/or fluoroscopy, cancer risk: 1748

LUNG NEOPLASMS

- epidemiology
 - occupational radiation exposure: 1755
 - smoking, historical review: 1714, 1715
 - therapeutic fluoroscopy and/or pneumothorax for TB, smoking: 1748
 - USSR (Moscow), TB: 2073

LYMPHOMA, MALIGNANT, EXPERIMENTAL (See also Virus, leukemia/lymphoma)

- canine, cellular transmission: 2112
- induction
 - methylnitrosourea, mouse: 1935
 - squirrel herpesvirus, marmoset: 2041, 2042
- reticulum cell sarcoma, outbreak, leukosis- and lymphoma-free colony of Japanese quail, Hawaii (Honolulu): 2051
- SJL/J mouse reticulum cell sarcoma, growth kinetics, theoretical model: 2050
- virus-induced lymphosarcoma, pathology, cat: 1964

LYMPHOMA, MALIGNANT, HUMAN

- associated congenital hypogammaglobulinemia, case (child) and review: 2107
- Burkitt
 - cell lines, properties: 2036, 2061, 2114
 - properties of transfer RNA: 2029
 - serum Epstein-Barr virus antibodies
 - intracellular and membrane antigen complexes: 2039
 - Japan and Taiwan: 2038
- epidemiology
 - Iran: 2092
 - New York, occupational asbestos exposure: 1763
 - Saudi Arabia (Dhahran), environmental factors: 2091
- Hodgkin's disease, epidemiology, world, review: 1726
- hydantoin anticonvulsants: 1909, 1910

LYMPHOMA, MALIGNANT, HUMAN (Contd.)

- occupational radiation exposure: 1755
- reticulum cell sarcoma, radiation-induced: 1745
- serum Epstein-Barr virus antibodies, West Germany (Essen): 2037

MALIGNANT TRANSFORMATION

- brain injury to brain tumor, child: 1738
- burn scar to cancer of skin: 1740
- chemical stenosis to cancer of esophagus: 1741
- chronic dental prosthesis irritation to cancer of hard palate: 1739
- familial polyposis to cancer of colon, enzyme histochemistry: 2103
- hereditary skin diseases, human: 1742
- irradiated lymph node to reticulum cell sarcoma: 1745
- radiation dermatitis to skin cancer: 1740, 1743
- therapeutic pneumothorax and/or fluoroscopy (for TB), lung cancer risk: 1748

MAMMARY CARCINOGENESIS, EXPERIMENTAL

- detergent additives (acenaphthenes), mouse or rat: 1772
- diethylstilbestrol, virus-like particles, rat: 2000
- dimethylbenzanthracene
 - mouse, virus-free preneoplastic nodules: 1836
 - rat: 1824, 1825, 1898
 - effect of portacaval shunt: 1823
 - hormone effects: 1821, 1822, 1824
 - virus-like particles: 2000
- formic acid 2-(4-[5-nitro-2-furyl]-2-thiazolyl)-hydrazide, mouse: 1907
- hydrazinotiazole compounds, rat: 1906
- methylnitrosourea, transplacental, rat: 1876
- methylcholanthrene (rat): 1898
 - virus-like particles: 2000
- oral contraceptive, rat: 1830
- radiation
 - rat: 1746
 - virus-free preneoplastic outgrowths, mouse: 1836
- trimethylbenzanthracene, rat: 1829
- urethan, virus-free preneoplastic outgrowths, mouse: 1836

MAMMARY CARCINOGENESIS, HUMAN

- benign fibroadenoma, oral contraceptives: 1806, 1831
- diethylstilbestrol, male: 1834

MAMMARY GLAND, EXPERIMENTAL

- dimethylbenzanthracene uptake, rat: 1826

MAMMARY NEOPLASMS, EXPERIMENTAL (See also Virus, mammary tumor)

- high- and low-frequency NZ mouse strains, review: 1712

spontaneous

- epidemiology, dogs, USSR (Moscow), genetic factors: 2098
- immunogenicity, virus-free mice: 2053
- transplantation, virus-positive to virus-free mouse strains: 1997

MAMMARY NEOPLASMS, HUMAN

- benign fibroadenoma, oral contraceptives: 1806, 1831

MMARY NEOPLASMS, HUMAN (Contd.)

epidemiology
hormone metabolism, review: 1724, 1725
India (Bombay), Hindus and Parsis: 2066, 2067
lactation and reproductive histories, Greece (Athens): 2079
pre- and postmenopausal patterns, Germany (Berlin): 2080
review: 1723
growth kinetics, mathematical model: 2100
herpesvirus-like particles: 2044
RIHUANA (See Cannabis)
LANOMA, MALIGNANT
epidemiology, Switzerland: 2076
familial (3 generations): 2077
genetics, review: 1718
transplantable, Type C virus particles, hamster: 1996
TALS, HEAVY
trace
analysis, human tumors: 1934
drinking water, cancer incidence, Italy (Pesaro): 2072
effect on benzpyrene hydroxylase, mouse lung: 1764

THENAMINE

toxicity, rat: 1922
THYLAZOXYMETHANOL (See Cycasin aglycone)
METHYLCHOLANTHRENE
benzpyrene hydroxylase induction, rat liver or hepatoma: 1904
effect on serum hemopexin, rabbit: 1903
liver tumors, enzymes, rat: 1902
mammary tumors (rat): 1898
virus-like particles: 2000
photodynamic effect, Neurospora or hamster cells: 1804
s.c. sarcoma, ultrastructure, mouse: 1900
skin tumors, virus-like particles, mouse: 1896
stomach tumors, effect of heated or unheated fats, guinea pig: 1899
transformed lung cultures, s.c. tumors, ultrastructure, mouse: 1897
uterine tumors, effect of hydroxynorprogesterone, mouse: 1901

THYLHYDRAZINE COMPOUNDS

chromosomal abnormalities, review: 1716

OTOMYCIN C (See under Antitumor agents)

OTOSIS

synchronization, effect on Rous sarcoma virus replication: 1941

OTH NEOPLASMS

hard palate, dental prosthesis: 1739

OTAGENESIS

chemical carcinogens, Drosophila: 1760
nitroquinoline oxide, bacteriophage: 1862

ELOMA AND RELATED DISEASES

plasmacytoma, associated solid tumors, cases and review: 1727
virus-like particles, mouse myeloma: 1988

NAPHTHYLAMINE

binding, DNA, RNA and protein, mouse liver or kidney: 1851
bladder tumors, rabbit: 1850

NAPHTHYLAMINE COMPOUNDS

reagents for bacterial nitrate reduction: 1773

NASOPHARYNX NEOPLASMS

epidemiology
Chinese, California: 2075
review: 1719
Taiwan and Japan, serum Epstein-Barr virus antibodies: 2038
serum Epstein-Barr virus antibodies intracellular and membrane antigen complexes: 2039
NEOPLASMS, EXPERIMENTAL
effect of physical or psychological stress, review: 1711
Ehrlich carcinoma (mouse)
cells, dimethylbenzanthracene binding: 1805
effect of nitroquinoline oxide on DNA: 1865, 1866

RAB-1 sarcoma (mouse), chloroleukemia-inducing virus: 1989
rat hepatoma
induced, glucuronyltransferase activity: 1902
transplanted, glucuronyltransferase activity: 1902
methylcholanthrene-induced benzpyrene hydroxylase: 1904

Sarcoma 180 (mouse), immunosuppression, Friend leukemia virus: 2064
spontaneous, epidemiology, dogs, USSR (Moscow): 2098

Walker 256 carcinosarcoma (rat), stimulation, electricity: 1750
Yoshida sarcoma (rat), effect of nitroquinoline oxide on nucleolus and chromosomes: 1864

NEOPLASMS, HUMAN (general and unspecified)

associated plantar or palmar keratoses: 2109
embryonic, association with congenital malformations, children: 2105
epidemiology
Armenian SSR (Chuvash): 2069
immunosuppression for kidney transplants: 2087
India (Bombay), ethnic groups (Parsis): 2066, 2067
Italy (Milan), age factors: 2096
New York and New Jersey, occupational asbestos exposure, review: 2071
socioeconomic status and smoking: 2070
South Africa (Johannesburg), ethnic groups: 2068

U.S., smoking, review: 2071
West Germany (Essen), serum Epstein-Barr virus antibodies: 2037

multiple, solid tumor(s) with leukemia: 1727, 1811

trace metal content: 1934

NEUROBLASTOMA

associated acute cerebellar encephalopathy, cases and review: 2104
familial, child: 2088

NERVOUS SYSTEM NEOPLASMS (See also Brain neoplasms)

transplacental induction
ethylnitrosourea, rat: 1880
methylnitrosourea, rat: 1876

NITRITE, SODIUM

heart, thymic, kidney or thyroid tumors, rat: 1882

NITROQUINOLINE COMPOUNDS

effect on crustacean eggs: 1861

4-NITROQUINOLINE 1-OXIDE

effect on

DNA, tumor cells: 1865, 1866

nucleolus and chromosomes, tumor cells: 1864

mutagenesis, bacteriophage: 1862

transformed cells, karyotype, hamster embryo cultures: 1863

NITROSAMINE COMPOUNDS

alkylnitrosamines, structure-activity relationship: 1867

chromosomal abnormalities, review: 1716

effect on crustacean eggs: 1861

NITROSAMINE, DIETHYL-

effect on glucuronide metabolism, animal: 1927

liver tumors, rat: 1869, 1928

NITROSAMINE, DIMETHYL-

effect on liver, trout, frog or bird: 1868

lung and liver tumors, mouse: 1870

toxicity

liver, rat: 1860

monkey or dog: 1871

NITROSO COMPOUNDS

teratogenesis, animal: 1859

N-NITROSOGUANIDINE, N-METHYL-N¹-NITRO-

effect on

DNA, rat tissues: 1872

SV40: 2033

stomach tumors, rat: 1873, 1874, 1875

N-NITROSOMORPHOLINE

liver tumors, rat: 1884

NITROSOPIPERAZINE, N,N¹-DI-

liver and lung tumors, mouse: 1883

N-NITROSOUREA, N-ETHYL-

brain tumors, sterol content, rat: 1881

CNS tumors, transplacental, rat: 1880

N-NITROSOUREA, N-METHYL-

brain tumors

rabbit: 1877, 1878

rat: 1876, 1877, 1880, 1881

effect on fetal brain, rat: 1876, 1879

lymphoma, mouse: 1935

transplacental tumor induction, rat: 1876

19-NORPROGESTERONE, 17 α -HYDROXY-

effect on methylcholanthrene uterine tumors, mouse: 1901

NUCLEIC ACIDS, DNA

adenovirus-2, denaturation pattern: 2059

binding

dimethylbenzanthracene, normal or tumor cells: 1801, 1805

 β -naphthylamine, mouse liver or kidney: 1851

skin carcinogens, mouse skin: 1921

effect of

aflatoxin: 1919, 1920, 1937

dimethylnitrosamine, normal tissues: 1868, 1870

hepatocarcinogens, rat liver: 1845, 1853, 1855, 1892, 1893

isoproterenol, rat salivary gland: 1930

methylnitro-N-nitrosoguanidine, rat tissues: 1872

nitroquinoline oxide, tumor cells: 1865, 1866

NUCLEIC ACIDS, DNA (Contd.)

Epstein-Barr virus, purification and properties: 2034, 2035

Moloney or Harvey sarcoma virus-infected or -transformed cells: 1956, 1958

polyoma-infected mouse cells, properties: 2012

Rous sarcoma virus-infected synchronized cells: 1941

SV40-transformed cells: 2025

NUCLEIC ACIDS, RNA

avian myeloblastosis virus, aminoacylation of component: 2054

benzanthracene-induced microsomal enzymes, hamster cells: 1828

binding

dimethylbenzanthracene, tumor cells: 1805

 β -naphthylamine, mouse liver or kidney: 1851

skin carcinogen, mouse skin: 1921

effect of

dimethylnitrosamine, trout, frog or bird liver: 1868

hepatocarcinogens, rat liver: 1853, 1855, 1893, 1920, 1937

mouse mammary tumor virus, isolation and properties: 2001

Rauscher leukemia virus-infected cells: 1944

Rous sarcoma virus (RSV-RAV1)-infected cells: 1944

transfer

BAI strain A virus and transformed cells: 1995

Burkitt lymphoma cells: 2029

normal or leukemic human WBC: 1968, 1970

SV40-infected cells or hamster tumor cells: 2029, 2030

NUCLEOLUS

effect of nitroquinoline oxide, tumor cells: 1864

SV40-infected human embryo cells: 2020

NUCLEOSIDES AND NUCLEOTIDES

oligonucleotides, effect of fluorenylacetamide: 1929

OCCUPATIONAL DISEASES

aromatic amine exposure, bladder cancer: 1782

asbestos exposure

bronchial cancer: 1762

cancer incidence, New York and New Jersey, review: 2071

leukemia/lymphoma, New York: 1763

mineral oil exposure, cancer of scrotum: 1767

radiation exposure, lymphoma or lung cancer incidence: 1755

skin cancer, medicolegal review: 1717

stomach cancer, pesticide exposure, case and review: 1720

2,6-OCTADIENAL, 3,7-DIMETHYL- (citral)

effect on benzpyrene-induced squamous metaplasia, hamster trachea *in vitro*: 1795

OILS, EDIBLE

sunflower oil, effect on fluorenylacetamide carcinogenesis, rat: 1842

OILS, MINERAL (See also Petroleum and petroleum products)

occupational exposure, cancer of scrotum: 1767

- PHORECTOMY (See under Endocrine ablation)
- OTIC ACID
effect on liver carcinogenesis, rat: 1847
- ARY NEOPLASMS
induction, ovarian autograft, rat: 1832
radiation-induced, mouse: 1754
- INCREAS NEOPLASMS
induction, oral contraceptive, rat: 1830
- ERYLENE
skin tumors, mouse: 1784
- STICIDES (See also Herbicides)
occupational exposure, cancer risk, case and review: 1720
- TROLEUM AND PETROLEUM PRODUCTS (See also Oil, mineral)
petrochemical effluents, benzantracene content, analytical method: 1827
processing, air pollution, bioassay method: 1791
- ENYLBUTAZONE
acute leukemia, genetic factors, human: 1911
toxicity, rat: 1922
- ORBOL ESTERS (See Croton oil phorbol esters)
- OSPHOLIPIDS
effect of hepatocarcinogen, rat liver: 1886
- TUITARY NEOPLASMS
induction, oral contraceptive, rat: 1830
mammatropic or mammosomatotropic, Type C virus particles, rat: 2000
- ANT PREPARATIONS
taenicides, liver cancer, Ethiopia: 2084
- ANTS
benzpyrene content, soil of low or high benzpyrene level: 1787, 1792
asmodium berghei yoelii
infection, effect on Harvey viral sarcoma, mouse: 1960
- ASTICS
premalignant cervical, uterine and vaginal lesions, mouse: 1836
- REGNANCY
reproductive histories, breast cancer incidence, Greece (Athens): 2079
ruptured placental membranes, benzpyrene diagnosis, human: 1798
transplacental carcinogenesis
ethylnitrosourea, rat: 1880
methylnitrosourea, rat: 1876
- ROGESTERONE
effect on dimethylbenzantracene mammary tumors, rat: 1824
- PROPIOLACTONE
skin tumors, mechanism, mouse: 1921
- ROSTATE NEOPLASMS
epidemiology, India (Bombay), ethnic groups: 2066
human, herpesvirus-like particles: 2044
- ROTEIN SYNTHESIS
benzantracene-induced microsomal enzymes, hamster cells: 1828
- ROTEINS
binding
dimethylbenzantracene, tumor cells: 1805
- PROTEINS (Contd.)
binding (Contd.)
hepatocarcinogens, rat liver: 1777, 1852, 1853, 1854, 1885, 1890, 1891
 β -naphthylamine, mouse liver or kidney: 1851
skin carcinogen, mouse skin: 1921
effect of dimethylnitrosamine, trout, frog or bird liver: 1868
paramagnetic complex, fluorenylacetamide liver tumor, isolation and properties, rat: 1848
SV40 capsid, analysis: 2031
- PROTOZOA
ameba, effect of aflatoxin: 1916
- PSYCHOLOGICAL FACTORS
effect on animal tumors, review: 1711
- Pteris aquilina
fractions, bladder tumors, mouse: 1781
- QUINOLINE, 4-HYDROXYAMINO-, 1-OXIDE
effect on DNA, tumor cells: 1865
transformation, chromosomes, hamster embryo cells: 1863
- RADIATION CARCINOGENESIS, EXPERIMENTAL
dose-response curve, mouse: 1754
effect of altitude, mouse: 1749
 γ -irradiation, effect of UV, mouse: 1744
mammary, rat: 1746
mouse: 1758
- RADIATION CARCINOGENESIS, HUMAN
cervix: 1737
occupational, lung cancer incidence: 1755
reticulum cell sarcoma, cancer radiotherapy-induced, cases: 1745
skin: 1740, 1743
therapeutic fluoroscopy (for TB), lung cancer, smoking: 1748
- RADIATION EFFECTS
chromosomal aberrations, atomic radiation exposure, Japan: 1757
laser, effect on DMBA-induced dyskeratosis, hamster cheek pouch: 1926
mouse cell cultures, sarcoma-forming effect and virus induction: 1752
polyoma-infected or transformed cells: 2010, 2014
stimulation of brain tumor, human: 1747
SV40-infected cells or hamsters: 1751
urethan-induced lung tumors, mouse: 1841
UV effect on γ -radiation tumorigenesis, mouse: 1744
virus-free preneoplastic mammary outgrowths, mouse: 1836
- RADIATION LEUKEMOGENESIS, EXPERIMENTAL
dose-response curve, mouse: 1754
effect of altitude, mouse: 1749
- RADIATION LEUKEMOGENESIS, HUMAN
Japan (Hiroshima, Nagasaki and other cities), clusters: 2095
residual bone marrow radioactivity, Hiroshima: 1756
- RADIOACTIVE ISOTOPES AND ELEMENTS
 ^{85}Sr and ^{90}Sr , retention, dosimetry, dog: 1753

RADIOMIMETIC COMPOUNDS

chromosomal abnormalities, review: 1716

RECTUM NEOPLASMS

pathogenesis, single- or multiple-"hit" mathematical model: 2085, 2086

RESERPINE

effect on fluorenyldiacetamide liver tumors, mouse: 1856

RESPIRATORY NEOPLASMS

epidemiology, India (Bombay), ethnic groups: 2066, 2067

RESPIRATORY TRACT

tracheobronchial tree, age-related gland development, conventional or germ-free mice: 2102

RETICULOENDOTHELIAL NEOPLASMS

possible induction by immunosuppressive therapy (kidney transplants): 2087

RIBOFLAVIN

effect on dimethylaminoazobenzene liver tumors, rat: 1940

SACCHARIN

bladder tumors, mouse: 1780

SAFROLE

liver and lung tumors, mouse: 1779

SALIVARY GLAND

DNA, effect of isoproterenol, rat: 1930

SALIVARY GLAND NEOPLASMS

induction

dimethylbenzanthracene, rat: 1812, 1814

fluorenylacetamide, effect of sunflower oil, rat: 1842

SCAR TISSUE (See also under Injuries)

brain injury malignant transformation, child: 1738

chemical burn stenosis, cancer of esophagus: 1741

radiation injury, malignant transformation, skin: 1740, 1743

therapeutic fluoroscopy and/or pneumothorax (for TB), cancer risk: 1748

varicose ulcer, malignant transformation, reticulum cell sarcoma after radiotherapy: 1745

SEROTONIN

fluorenylenebisacetamide-induced liver and intestinal tumors, rat: 1857

SEX DIFFERENCE

colon/rectum cancer mortality, theoretical model: 2086

fluorenyldiacetamide liver tumors, mouse: 1856

SKIN

abnormal dermatoglyphic patterns, children with retinoblastoma: 2108

benzpyrene distribution, mouse: 1794

dimethylbenzanthracene absorption, mouse: 1815

intraepidermal nerve fibers, effect of dimethylbenzanthracene, mouse or rabbit: 1818

plantar or palmar seed keratoses, cancer pts. and normal subjects: 2109

transplantation, graft survival time, mouse with urethan-induced lung tumors: 1838

SKIN CARCINOGENESIS

aromatic hydrocarbons and phorbol ester, mouse: 1784

arsenic, human: 1776

dimethylbenzanthracene

hamster cheek pouch: 1802, 1813, 1926

mouse: 1803, 1815

fluorenylacetamide, effect of sunflower oil, rat: 1842

γ -irradiation, effect of UV, mouse: 1744

methylcholanthrene, virus-like particles, mouse: 1896

β -propiolactone, mechanism, mouse: 1921

radiation, human: 1743

s.c. tumors

dimethylbenzanthracene, hamster: 1816

hydroxycholesten-3-one, mouse: 1936

methylcholanthrene, mouse: 1900

oral contraceptive, rat: 1830

transplanted methylcholanthrene-treated lung cultures, mouse: 1897

scrotum, occupational mineral oil exposure: 1767

tobacco smoke extracts, mouse or hamster: 1784, 1802, 1803

SKIN DISEASES

familial, malignant transformation: 1742

SKIN NEOPLASMS

epidemiology

dogs, USSR (Moscow): 2098

India (Bombay), Hindus and Parsis: 2066, 2067

occupational, medicolegal review: 1717

transformation of

radiation dermatitis: 1740, 1743

scar tissue: 1740, 1745

xeroderma pigmentosum, cases: 1742

SOCIOECONOMIC FACTORS

cancer epidemiology, relationship to smoking habits: 2070

cervix cancer, review: 1721

SOIL

benzpyrene content, industrial or rural region, USSR: 1787, 1792

SPLEEN

dimethylbenzanthracene-DNA binding, rat: 1801

gallium distribution, leukemic or nonleukemic AKR/J mice: 1775

STATOLON

effect on Friend viral leukemia, mouse: 1971

STEROLS

analysis, ethyl- or methylnitrosourea-induced brain tumors, rat: 1881

STOMACH

DNA methylnitro-N-nitrosoguanidine uptake, rat: 1872

STOMACH NEOPLASMS

association with peptic ulcer and atherosclerosis: 2110

epidemiology

air pollution, bioassay method: 1791

Iceland, dietary factors: 2083

induction

benzpyrene, mouse: 1791

GASTROINTESTINAL NEOPLASMS (Contd.)

- induction (Contd.)
 fluorenylacetylamide, effect of sunflower oil, rat: 1842
 methylcholanthrene, effect of heated or unheated fats, guinea pig: 1899
 N-methyl-N'-nitro-N-nitrosoguanidine, rat: 1873, 1874, 1875
 occupational pesticide exposure, case and review: 1720
 PRESS (See also under Injuries)
 effect on animal tumors, review: 1711
 electrical current, tumor stimulation, rat: 1750
 SUNFLOWER OIL (See under Oils, edible)
 T40 (See under Virus, papova)

TEMPERATURE

- sensitive mutants of avian sarcoma virus (B77), properties: 1962
 TERATOGENESIS (See also under Embryo)
 aflatoxins, alkylating agents and nitroso compounds, animal: 1859
 benzanthracene derivatives, structure-activity relationship, rat: 1807
 TESTOSTERONE, 2 α -METHYLDIHYDRO-
 effect on DMBA mammary tumors, rat: 1822
 TESTOSTERONE PROPIONATE
 effect on DMBA mammary tumors, rat: 1822
 TESTOSTERONE PROPIONATE + DIETHYLSTILBESTROL
 implantation, uterine leiomyosarcoma, hamster: 1833

THYMUS

- gallium distribution, leukemic or nonleukemic AKR/J mice: 1775
 Gross leukemia virus-transformed rat cells, pathology: 2065
 thymectomy
 effect on dimethylbenzanthracene leukemogenesis, mouse: 1809
 urethan-induced lung tumors, mouse: 1841

THYMUS NEOPLASMS

- induction, dimethylurea + nitrite, rat: 1882

THYROID NEOPLASMS

- epidemiology, Hawaii (Oahu): 2074
 induction, dimethylurea + nitrite, rat: 1882

TOBACCO

- carcinogens, chromosomal abnormalities, review: 1716
 cocarcinogens, cell culture test: 1761
 extracts, antigenicity (human serum): 1769
 TOBACCO SMOKE
 containing Cannabis constituents, analysis: 1765

TOBACCO EXTRACTS

- lung tumors, mouse: 1768
 skin tumors, mouse: 1784, 1803
 tumor promotion, hamster cheek pouch: 1802

TOBACCO SMOKING

- cancer incidence
 India (Bombay), Hindus and Parsis: 2066, 2067
 relationship to socioeconomic status: 2070
 review: 1714, 1715
 U.S., review: 2071

TOBACCO SMOKING (Contd.)

- effect on
 asbestosis induction, review: 1713
 mucociliary efficiency of lung, human: 1770
 lung cancer, treated TB: 1748
 TOXICITY
 aflatoxin (liver)
 human: 1914
 monkey: 1913
 mouse: 1915, 1938
 rat: 1938
 cycasin aglycone, mouse or rat: 1924
 dimethoxyaminoazobenzene, rat: 1889
 dimethylnitrosamine, monkey or dog: 1871
 hepatocarcinogens, liver, mechanism, rat: 1860
 methenamine, rat: 1922
 phenylbutazone, rat: 1922

TRACHEA

- benzpyrene-induced squamous metaplasia, effect of citral or vitamin A in vitro, hamster: 1795

TRANSPLACENTAL CARCINOGENESIS (See under Pregnancy)

TRYPTOPHAN METABOLITES

- metabolism, animal: 1931, 1932

ULCER, PEPTIC

- association with stomach cancer and atherosclerosis: 2110

UREA, DIMETHYL-

- heart, thymic, kidney or thyroid tumors, rat: 1882

URETHAN

- effect on virus-free preneoplastic mammary outgrowths, mouse: 1836
 lung tumors (mouse): 1778, 1838, 1839, 1840
 effect of thymectomy and radiation: 1841
 with virus-containing leukemia: 1991

UTERUS (See Corpus uteri)

VAGINA NEOPLASMS

- induction, plastics, mouse: 1836

VINBLASTINE (See under Antitumor agents)

VIRAL CARCINOGENESIS

- animal, review: 1728
 DNA viruses
 chromosomes, review: 1732
 nuclear antigens, review: 1731
 genetic factors, theory, review: 1729
 human adenoviruses, mechanism, review: 1730

VIRUS

- arbovirus, cytolytic effects, mouse leukemia cells: 2049
 infectious parotitis or Sendai, effect on defective Rous sarcoma virus: 1949
 lymphocytic choriomeningitis, effect on autoimmunity, NZB mice: 2063
 parvovirus H-1, effect on adenovirus-12-infected human embryo cells: 2004

VIRUS, ADENO-

- canine A26/61 (respiratory-associated)
 hamster tumors: 2006
 human
 mechanism of action, review: 1730

VIRUS, ADENO- (Contd.)

- Type 2
 - DNA denaturation pattern: 2059
 - enhancement by SV40, monkey kidney cells: 2056
- Type 5
 - capsid proteins, synthesis and morphogenesis: 2055
- Type 7
 - oncogenic (hamster) strains, properties: 2005
- Type 12
 - degradation and integration, abortively-infected hamster cells: 2057
 - hamster tumors, membrane transplantation antigen, properties: 2003
 - infected human embryo cells, effect of parvovirus (H-1): 2004
 - inhibition of benzpyrene tumors, hamster: 1925
 - transformation, estrogen enhancement, hamster cells: 2002

VIRUS, HERPES

- cervix cancer, review: 1721
- simplex
 - attempted EB virus rescue, Burkitt lymphoma cell lines: 2061
- squirrel (Herpesvirus saimiri)
 - lymphoma induction, marmoset: 2041, 2042
 - properties: 2040
- Type 1 (oral)
 - serum antibodies, cervix cancer: 2043
- Type 2 (genital)
 - serum antibodies, cervix cancer: 2043

VIRUS, HERPES-TYPE

- Epstein-Barr (human)
 - Burkitt lymphoma cell lines
 - attempted rescue (herpes simplex virus): 2061
 - properties: 2036, 2114
 - DNA, purification and properties: 2034, 2035
 - nasopharynx cancer, Chinese and other Oriental populations, review: 1719
 - serum antibodies
 - cancer pts., West Germany (Essen): 2037
 - intracellular and membrane antigen complexes: 2039
 - nasopharynx cancer and other tumors, Japan and Taiwan: 2038
- Lucké (frog kidney tumor)
 - particles resembling, human prostate and breast cancer: 2044

VIRUS, LEUKEMIA/LYMPHOMA

- AKR (mouse)
 - gallium distribution, leukemic or nonleukemic AKR/J mice: 1775
 - sensitivity, strain differences, mouse: 1983
- AKR/J (mouse)
 - excretion, AKR/J, C58/J and SJL/J mice: 1979
- avian leukosis
 - effect on defective Rous sarcoma virus: 1949
 - subgroup A (RAV-1), interference with Rous sarcoma virus: 1947
 - subgroup B (RAV-2), interference with Rous sarcoma virus: 1947
 - subgroup C (RAV-50), interference with Rous sarcoma virus: 1947

VIRUS, LEUKEMIA/LYMPHOMA (Contd.)

- avian leukosis (Contd.)
 - virus-free colony of Japanese quail, reticulum cell sarcoma outbreak: 2051
- avian myeloblastosis
 - RNA components, aminoacylation: 2054
- BAI strain A (avian myeloblastosis)
 - transformed cells, properties of transfer RNA: 1995
- cat
 - infectivity, human cells: 1965
- Friend (mouse)
 - antibody formation, mouse, rat or rabbit: 1976
 - detection, method, mouse cell cultures: 1973
 - immunosuppression, normal or tumor-bearing mouse: 1972, 2064
 - infection, effect of inhibitor, mouse: 1977
 - latent infection after suppression, mouse: 1971
 - polycythemia-inducing strain, properties: 1974
 - splenic focus-forming strains, properties: 1974, 1975
 - susceptibility, effect of Rich virus-induced lymphoma, mouse: 2047
- Graffi (mouse)
 - chromosomes, review: 1735
 - tissue graft from resistant (XVII/G) to sensitive (C57BL) strain, leukemia induction: 1992
- Gross (mouse)
 - host immunity, non-leukemic AKR mice: 1982
 - transformed rat thymus cells, pathology: 2065
- human
 - possible, leukemia clusters, Japan: 2095
- Mazurenko (mouse)
 - detection, mouse cell cultures: 1973
- MC29 avian leukosis
 - infected chick embryo cells, mesothelioma induction, chicken: 1994
- Moloney (mouse)
 - rescue, MSV-33 rat-adapted sarcoma virus pseudotype: 1980
- mouse
 - chloroleukemia, induction and transplantation: 1989
 - chromosomal anomalies, review: 1734
 - detection, lymphosarcoma of "starry-sky" histology: 1966
 - induction, sarcomas from irradiated cell cultures: 1752
 - intracellular Type A2 particles, urethane-induced leukemia and lung tumor, mouse: 1991
 - isolation, bones of high-leukemia mouse strains (AKR and C3H/Fg): 1981
 - myeloid leukemia, isolation, methods: 1985, 1986
 - tissue antigens, mouse: 1987
 - particles resembling, mouse myeloma cells: 1988
 - SJL/J reticulum cell neoplasms, transmission and biological activity: 1984
- rat leukemia
 - Type C particles: 1990

US, LEUKEMIA/LYMPHOMA (Contd.)

Rauscher (mouse)

effect on

autoimmunity, NZB mice: 2048

lymphocytic stimulation response, mouse:
1978

infection, effect of inhibitor, mouse: 1977

rat-adapted sarcoma virus pseudotype (MSV-33),
rescue and virus-specific antigenicity:
1980

RNA synthesis pattern, infected cells: 1944

tumor pathology: 2046

Rich lymphoma (mouse)

effect on Friend leukemia virus suscepti-
bility, mouse: 2047

Type C particles

pituitary mammatropic or mammosomatotropic
tumors, rat: 2000transplantable pigmented hamster melanoma:
1996urethan-induced leukemia and lung tumor,
mouse: 1991

US, MAMMARY TUMOR

Bittner (mouse)

direct cell-to-cell transfer, C3H mouse
mammary tumors: 1999

structure and properties: 1998

mouse

isolation and properties of RNA: 2001

tumor transplantation from virus-positive
to virus-positive or virus-free strains:
1997virus-free mice, immunogenicity of spon-
taneous mammary tumors: 2053nodular outgrowths, effect of radiation
or carcinogens: 1836

rat

dimethylbenzanthracene-, methylcholanthrene-,
or diethylstilbestrol-induced mammary
tumors: 2000

Type A particles

methylcholanthrene-induced skin tumors,
mouse: 1896

US, PAPOVA (papilloma-polyoma-vacuolating)

polyoma

effect on autoimmunity, NZB mice: 2063

hamster tumors

effect of immune serum: 2058

host immunity: 2013

strain differences in pathology (CET
and RTT viruses): 2016, 2017

infected cells

effect of UV or actinomycin: 2014

histone synthesis: 2018

properties of cellular DNA: 2012

low-tumor clones, antigenicity, transformed
hamster cells: 2011

mouse tumors, host immunity: 2015

properties of virion: 2008

runtig, effect of immune serum, hamster:
2058temperature-sensitive mutant, properties:
2009

transformed cells

collagen:galactosyl transferase distri-
bution: 2019VIRUS, PAPOVA (papilloma-polyoma-vacuolating)(Contd.)
polyoma (Contd.)

transformed cells (Contd.)

endonuclease, properties: 2060

UV- or mitomycin C-induced virus synthesis:
2010

Shope papilloma

masking, mechanism, rabbit tumors: 2007

properties of virion: 2008

SV40

adenovirus-5 enhancement, monkey kidney cells:
2056

capsid proteins, analysis: 2031

defective, transformation, mouse cells: 2028

effect of nitrosoguanidine compound: 2033

hamster tumors

detection of SV40 antigens, host WBC:
2023

properties of transfer RNA: 2029

T and tumor antigens: 2021

infected cells

histone synthesis: 2018

human embryo, nucleoli: 2020

pseudovirus production, monkey cells: 2032

radiation effects, infected cells or hamster:
1751

transformation

BSC-1 monkey kidney cells: 2026, 2027

role of DNA synthesis, monkey kidney
cells: 2025

transformed cells

collagen:galactosyl transferase distri-
bution: 2019

hamster, mouse or rat, properties: 2022

membrane-specific antibodies: 2062

mitomycin C induction: 2024

VIRUS, SARCOMA

B77 (avian)

rat-adapted strain, properties: 1963

temperature-sensitive mutants, properties:
1962

transformation, rat cells: 1963

cat

C-type, isolation and pathogenicity: 1964

infectivity, human cells: 1965

hamster

reticulum cell sarcoma: 2052

Harvey (mouse)

effect of Plasmodium berghei yoelii infection,
mouse: 1960infected cells, effect of DNA antimetabolite:
1958

pathology and virus yield: 1957

transformed cells

plasma membrane properties: 1959

growth rates: 1961

tumor growth kinetics, theoretical model:
2050

Mill Hill-2 reticuloendothelioma (chicken)

classification and genetic resistance:
1950

Moloney (mouse)

effect of antimetabolite, infected mouse
cells: 1956

infection, effect of inhibitor, mouse: 1977

pathology and virus yield, mouse: 1957

SUBJECT INDEX

VIRUS, SARCOMA (Contd.)

Moloney (mouse) (Contd.)

transformed mouse cells

effect of antimetabolite: 1956

interferon: 1955

tumor growth kinetics, theoretical model: 2050

MSV-33 pseudotype (rat)

rescue and virus-specific antigenicity: 1980

Rous (chicken)

Bryan strain

defective effect of Rous-associated or avian leukosis virus: 1949

replication, synchronized cells: 1941

transformed cells, surface properties: 1942

Engelbreth-Holm strain

transformed human cells (EH-118MG),

properties: 1951

Harris strain

defective, properties: 1948

interference with RSV- β (0): 1947

Prague strain

mouse tumors, properties: 1952

RSV(0)

envelope properties: 1943

helper virus-free, infectivity, birds: 1946

RSV- β (0)

helper virus-free, interference with avian leukosis viruses: 1947

RSV-RAV1

RNA synthesis, infected cells: 1944

VIRUS, SARCOMA, Rous (Contd.)

transformation, effect of medium, chick embryo cells: 1945

Schmidt-Ruppin strain

leukemoid reaction, conventional or

germ-free rat: 1953

mouse tumors, properties: 1952, 1954

Rous-associated (chicken)

effect on defective Rous sarcoma virus: 1949

VITAMIN A

effect on benzpyrene-induced squamous metaplasia, hamster trachea in vitro: 1795

WATER POLLUTION

benzanthracene, petrochemical effluents,

analytical method: 1827

benzpyrene, method of removal: 1788

polycyclic aromatic hydrocarbons, analysis, method: 1785

WATER SUPPLY

trace metal content, cancer incidence, Italy (Pesaro): 2072

XANTHURENIC ACID 8-METHYL ETHER

metabolism, rabbit: 1932

ZINC DIMETHYLDITHIOCARBAMATE

lung tumors, mouse: 1778

ZINC ETHYLENE-BIS(DITHIOCARBAMATE)

lung tumors, mouse: 1778

U.S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

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EMBER-DECEMBER 1970

Abstract Nos. 2115-2672

**Vol.8
Nos. 11-12**

CARCINOGENESIS ABSTRACTS

National Cancer Institute

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE • National Institutes of Health

CARCINOGENESIS ABSTRACTS

Volume 8, Issue 11-12

Abstract Numbers
2115-2672

CONTENTS

	<u>Page</u>
Review	399
Physical Carcinogenesis	405
Chemical Carcinogenesis	410
Viral Carcinogenesis	442
Epidemiology and Biometry	483
Miscellaneous	506
Author Index	i
Subject Index	viii

Prepared by Scientific Literature Corporation
(A Subsidiary of the 3i Company)
Philadelphia, Pennsylvania 19103

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Pursuant to a Contract with the Public Health Service
U.S. Department of Health, Education and Welfare

PH43-70-2036

Use of funds for printing this publication approved
by the Director of the Bureau of the Budget on July 25, 1967.

FOREWORD

The National Cancer Institute, in response to Congressional interest and desire for a national program of cooperative research in cancer, is establishing a means whereby information in the field of carcinogenesis will be coordinated and made available. The information to be included will be obtained from the National Cancer Institute, other governmental agencies, and non-governmental research institutions.

The issuing of Carcinogenesis Abstracts under the auspices of the National Cancer Institute will provide a central source for current abstracting of the carcinogenesis literature being published throughout the world. This will help facilitate an integrated and cooperative program of investigation in this area. The growing number of publications in the area of carcinogenesis makes imperative the availability of an appropriate abstracting service so that investigators may be apprised of progress with a minimum of delay. It is our desire to provide the investigator with a readily systematized compilation of the published work.

Carcinogenesis Abstracts will be published monthly and will include abstracts from the most recently published literature.

Inquiries may be addressed as follows:

Carcinogenesis Abstracts
National Institutes of Health
National Cancer Institute
Bethesda, Maryland 20014

NOTE

Journal names are abbreviated according to the list of abbreviations used by Index Medicus. If the journal is not covered by Index Medicus, then the abbreviations (with some modifications) found in World Medical Periodicals, 3rd Edition, are used.

ABBREVIATIONS USED IN ABSTRACTS

admin.	administered, administration	mg	milligram(s)
av.	average	min.	minute(s)
	curie(s)	ml	milliliter(s)
C	millicurie(s)	mm	millimeter(s)
C	microcurie(s)	mo.	month(s)
m	centimeter(s)	MTD	maximum tolerated dose
onc.	concentration	NIH	National Institutes of Health, USA
pm	counts per minute	p.o.	orally
NA	deoxyribonucleic acid	QO ₂	oxygen quotient
Nase	deoxyribonuclease	PFU	plaque forming unit
g.	for example	ppm	parts per million
FU	focus forming unit	pt.(s)	patient(s)
i.	gastrointestinal	RBC	red blood cells (erythrocytes)
	gram(s)	RES	reticuloendothelial system
g	microgram(s)	resp.	respectively
	hemoglobin	RNA	ribonucleic acid
a.	intra-arterial	RNase	ribonuclease
50	median infectious dose	soln.	solution
ij.	injected, injection(s)	s.c.	subcutaneous
oc.	inoculated, inoculation(s)	TCID	tissue culture infectious dose
p.	intraperitoneal	x	times (e.g. x 3/wk.)
U.	international unit(s)	U	unit
v.	intravenous	UV	ultraviolet
	kilogram(s)	vol.	volume
50	median lethal dose	VA	Veterans Administration
	molar, mole(s)	wt.	weight
	millimole(s)	WBC	white blood cells (leukocytes) or white blood cell count
	micromole(s)		
ix.	maximum	yr.	year(s)

LANGUAGE ABBREVIATIONS

Afrikaans	E.	English	Hun.	Hungarian	Lith.	Lithuanian	Ser.	Serbo-Croatian
Arabic	Eston.	Estonian	lc.	Icelandic	Maced.	Macedonian	Sl.	Slovene
Bulgarian	Fin.	Finnish	ln.	Indonesian	Nor.	Norwegian	Sp.	Spanish
Chinese	Fr.	French	lt.	Italian	Pol.	Polish	Sw.	Swedish
Czech	Ger.	German	Jap.	Japanese	Por.	Portuguese	Th.	Thai
Danish	Gr.	Greek	Kor.	Korean	Rum.	Rumanian	Uk.	Ukrainian
Dutch	Heb.	Hebrew	Latv.	Latvian	Rus.	Russian	Viet.	Vietnamese

2115 TOBACCO AND CANCER: THE FIRST CLINICAL REPORT, 1761. (E.) Redmond, D. E., (1601 W. Taylor St., Chicago, Ill.). New J. Med. 282(1):18-23, 1969. (77 references)

The use of tobacco and snuff for therapeutic, medicinal and pleasure purposes and their association with cancer are reviewed. Dr. John Hill's first report (1761), with 6 reports of polyps or cancer of the nasal cavity in habitual snuff-takers, is discussed.

2116 TUMORIGENIC AGENTS IN THE HUMAN ENVIRONMENT AND SOME MECHANISMS OF CARCINOGENESIS. (Rus.) Shabad, L. M. (Sci. Res. Inst. Clin. Oncol., Moscow). Vestn. Akad. Med. Nauk SSSR 24(6):3-13, 1969. (18 references)

The presence of 3,4-benzpyrene and other carcinogenic hydrocarbons (CH) in airplane exhaust gas, the soil and vegetation at airports, in water and in tars used in the manufacture of ointments for treating skin disease was studied. Research on the metabolism of CH by microorganisms in vitro and in vivo, the effects of griseofulvin on carcinogenesis in animals, and the effects of methan, N-methylnitrosoamine and dimethylnitrosamine on tissue cultures from embryos of these mothers had been treated with these substances is also reviewed.

2117 BLOOD VESSELS IN SARCOMAS INDUCED BY PLASTICS. (Rus.) Krylova, N. V. (Lumpava People's Friendship U., Moscow) and A. Kh. Vestn. Acad. Med. Nauk SSSR 24(6):10, 1969. (20 references)

Research on the blood supply to the capsule of connective tissue which surrounds Teflon and "Vinylrose" implanted under the skin of male noninbred rats is presented. The role of circulatory disturbances, such as increased capillary formation, thrombosis and venous and capillary deformation, in the malignant transformation of these capsules to sarcomas is discussed.

2118 HEPATIC CARCINOGENESIS. (E.) Burdette, W. J. (U. Texas M. D. Anderson Hosp. Cancer Inst., Houston). Recent Results Cancer Res. 26:53-71, 1970. (147 references)

Evidence supporting the major significance of environmental factors in primary hepatic neoplasms is presented. Included in discussion are dyes, selenium, aromatic amines, nitrosamine, activation of hepatocarcinogens, polycyclic aromatic hydrocarbons, the relation of cirrhosis to hepatic carcinoma, hepatocarcinogens from fungi and bacteria and carcinogenic compounds in plants.

2119 FACTORS INFLUENCING MALIGNANCY VERSUS BENIGNANCY OF THYROID NEOPLASMS IN MAN

AND EXPERIMENTAL ANIMALS II - EXPERIMENTAL ANIMALS. Money, W. L. and R. W. Rawson. Pp. 179-199 in Thyroid Neoplasia, Young, S. and D. R. Inman (Eds.). Academic Press, London, 1968, 470 pp. (41 references)

A review of transplantable thyroid tumors in Sprague-Dawley rats, Fischer rats and Syrian hamsters is concerned with the problem of transplantability, histological transformation and functional activity of the tumors. Six specific problems are discussed: The type of tissue which will "take" when transplanted and the thyroid status of the recipient; histological transformation of the tumors during passage; factors influencing growth of implanted tumor tissue; biological ¹³¹I turnover by the tumors; the iodinated compounds produced by transplantable thyroid tumors; and the deiodination of labeled compounds by transplantable thyroid tumors.

70-2120 MORPHOLOGY OF THE ADENOHYPOPHYSIS ADRENAL SYSTEM AND HORMONAL CARCINOGENESIS. (Rus.) Zhuravleva, T. B. (Leningrad 1st Med. Inst., USSR). Ark. Pat. 32(4):13-25, 1970. (153 references)

The role of hormones, particularly estrogens, in carcinogenesis and adrenal response to these hormone imbalances are discussed, with reference to the non-Soviet literature. Limitations of morphological and histological methods in investigating the adenohypophysis-adrenal system and differences in the responses of different species to high estrogen levels are discussed.

70-2121 ACTION OF AFLATOXIN ON MICROBIAL CELLS. (Fr.) Jacquet, J. (Microbiol. Lab., Caen, France) and P. Boutibonnes. C. R. Soc. Biol. (Paris) 163(12):2574-2578, 1969. (12 references)

The toxic effects of aflatoxin (produced by Aspergillus flavus) on viruses, bacteria and fungi are discussed, in relation to the formation of monstrosities of the sporangiophores and vegetative hyphae, and the development of a dense rubbery mycelium, in proportion to the conc. of toxin produced.

70-2122 ADAPTATION OF CELLULAR CONTROL PROCESSES IN RELATION TO CANCER AND ITS THERAPY. (E.) Harington, J. S. (South African Inst. Med. Res. Cancer Unit, Johannesburg). J. Theor. Biol. 28(1):31-45, 1970. (92 references)

The possibility that cancer results from adaptive disturbances in the oscillatory properties of certain regulatory pathways due to carcinogens is reviewed, with special reference to an explanation of uncontrolled cell division by changes in the control of biosynthesis of glutathione. The re-adaptation of disturbed systems (restoration of altered regulatory

activity, artificial alteration of oscillation in metabolic systems and natural control of feedback biosynthesis) in cancer is also discussed.

- 70-2123 STUDIES ON THE CELLULAR AND MOLECULAR MECHANISMS OF HYDROCARBON CARCINOGENESIS. (E.) Heidelberger, C. (U. Wisconsin Med. Sch. McArdle Lab. Cancer Res., Madison). Europ. J. Cancer 6(3):161-172, 1970. (61 references)

Topical application of carcinogenic hydrocarbons (CH) to mouse skin was performed in studies on the carcinogenic process and the interaction of CH with DNA, RNA and proteins. Cells from the ventral prostate of C3H mice were used in a quantitative study of malignant transformation *in vitro*. It is concluded that the carcinogenic mechanism does not involve selection of pre-existent malignant cells.

- 70-2124 MECHANISMS OF CARCINOGENESIS. (E.) Brues, A. M. (Argonne Nat. Labs., Argonne, Ill.), H. Auerbach, G. M. DeRoche and D. D. Grube. Argonne Nat. Labs. Ann. Rep. ANL-7635:115-119, 1969. (14 references)

DNA synthesis in the dorsal epidermis of the hairless mouse was studied during different periods of the day using ^{14}C or ^3H -labeled thymidine. Results show that the flux of cells from growth phase I into synthesis phase was actually changing and that this change was sufficient to cause the diurnal rhythm in the number of cells in DNA synthesis and in subsequent portions of the mitotic cycle. Attempts to demonstrate promotion of mouse skin carcinogenesis by croton oil extracts after external β -irradiation failed. Tumor induction in rats by non-radioactive materials, such as different types of Millipore filters, is also being investigated in relation to pore size and surfactant effects.

- 70-2125 CELLULAR PROLIFERATION AND CARCINOGENESIS. (E.) Reiskin, A. B. (Argonne Nat. Labs., Argonne, Ill.) and A. R. Sallèse. Argonne Nat. Labs. Ann. Rep. ANL-7535:35-37, 1968. (7 references)

The *in vivo* proliferative behavior of the epithelial lining of the hamster cheek pouch is reviewed as a function of different physiological responses (aging, diurnal rhythms, transplantation) and in relation to the effects of different carcinogenic stimuli (chemicals, irradiation). Results suggest substantial mitotic changes in the cell regeneration cycle and time-dependent behavioral differences in relation to diurnal and circadian rhythms.

- 70-2126 CELLULAR PROLIFERATION AND CARCINOGENESIS. (E.) Reiskin, A. B. (Argonne Nat.

Labs., Argonne, Ill.) and A. R. Sallèse. Argonne Nat. Labs. Ann. Rep. ANL-7635:121-126, 1969. (3 references)

Cell growth kinetics of normal and tumor tissues of various experimental animals under varied conditions (such as temperature change and altered physiological conditions which effect proliferative behavior) and after attempted tumor induction by X-irradiation or viral inoc. are reviewed.

- 70-2127 AUTORADIOGRAPHIC STUDIES OF REGENERATION AND CARCINOGENESIS. (Ger.) Oehlert, W. (U. Freiburg Path. Inst., Germany). Acta Histochem. (Jena) 8(Suppl.):257-274, 1968. (28 references)

A review, which often refers to the author's previous publications and those of his associates, illustrates the use of ^3H -thymidine in autoradiographic studies of regeneration and radiation or chemical carcinogenesis in animal and human tissues (especially the skin and intestinal mucosa).

- 70-2128 TRANSPLACENTAL ACTION OF TUMORIGENIC AGENTS ON ORGAN CULTURES. (Rus.) Shabad, L. M. (Inst. Exp. Clin. Oncol., Moscow). Pat. Fiziol. Eksp. Ter. 14(2):28-33, 1970. (20 references)

The effects of urethan, N-nitrosomethylamine, N-nitroso-N-methylurea, 7,12-dimethylbenzanthracene, 3,3'-dichlorobenzidine and hexachlorocyclohexane, admin. to pregnant mice, on kidney and lung cultures made from their embryos are reviewed. Epithelial hyperplasia and metaplasia produced by these tumorigenic agents are considered precancerous in nature.

- 70-2129 CARCINOGENESIS AND TERATOGENESIS. (Ger.) von Kreybig, T. (Mohlstr. 54, Tübingen, Germany). Arzneimittelforschung 20(5):591-601, 1970. (73 references)

Typical teratogenic processes which follow treatment with cytostatic and other alkylating teratogenic substances are described and cellular processes in carcinogenesis such as the biochemical primary process (transformation of the cellular regulatory system resulting in the development of potential tumor cells), latent period, tumor growth and development of metastases are discussed. The relationship between transplacental carcinogenesis and teratogenesis was analyzed and it is concluded that in only rare instances can a definite correlation between carcinogenesis and teratogenesis be established.

- 70-2130 SELECTION OF THE VALID NUMBER OF SAMPLING UNITS AND A CONSIDERATION OF THEIR COMBINATION IN TOXICOLOGICAL STUDIES INVOLVING REPRODUCTION, TERATOGENESIS OR

CARCINOGENESIS. (E.) Weil, C. S. (Carnegie-
ellon U., Pittsburgh, Pa.). Food Cosmet. Toxic.
(2):177-182, 1970. (6 references)

mathematical model is presented for correct
statistical analysis of data pertaining to
reproduction studies and toxicological, teratogenic
or carcinogenic experiments. Emphasis is placed
on the ease in which errors are made due to
an invalid number of sampling units or exaggeration
of significance.

2131 RADIATION CARCINOGENESIS. (E.) Warren,
S. (Harvard Med. Sch., Boston, Mass.).
NY Acad. Med. 46(3):131-147, 1970.
(33 references)

a variety of forms of ionizing radiation, including
exposure to radioactive fallout, radiation
therapy, occupational exposure and cases of
survivors of the atomic bomb in Japan, are re-
viewed in relation to the development of cancer.
Dose-effect relations are possibly correlated
with a higher incidence rate. A multiple
mechanism for radiation carcinogenesis is suggested.

2132 THE EXPERIMENTAL PRODUCTION OF THYROID
NEOPLASMS IN THE RAT BY IRRADIATION.
Mandsay, S. Pp. 279-289 in Thyroid Neoplasia,
Young, S. and D. R. Inman (Eds.). Academic Press,
London, 1968, 470 pp. (30 references)

The pathogenesis of thyroid neoplasms induced in
rats by irradiation with either ¹³¹I or X-rays
and the various factors (including thyroidectomy,
partial lobectomy, or diets containing propyl-
thiouracil or desiccated thyroid powder or both)
that may in some fashion modify the neoplastic
response to irradiation are reviewed.

2133 MALIGNANT TUMOURS OF THE THYROID GLAND
AND EXTERNAL FACTORS. Lea, A. J. Pp.
9-256 in Thyroid Neoplasia, Young, S. and D. R.
Inman (Eds.). Academic Press, London, 1968,
470 pp. (6 references)

Statistical investigation by the World Health
Organization concluded that there is a negative
association between consumption of fish in the
diet and cancer of thyroid, and a positive
association between drinking milk and cancer of
the thyroid, possibly acting through the inter-
mediate stage of a simple goiter. Certain
features of endemic goiter led to the theory that
cancer of the thyroid is a preventable disease.

2134 ALPHA-FETOPROTEIN: OCCURRENCE IN
CERTAIN MALIGNANT DISEASES AND REVIEW
OF CLINICAL APPLICATIONS. (E.) Smith, J. B.
U.S. Naval Med. Ctr., Bethesda, Md.). Med.
in. N. Amer. 54(3):797-803, 1970.
(10 references)

The globulin, α -fetoprotein, was found in the
sera of 50-79% of pts. with hepatocellular
carcinoma, as well as in some pts. with embryonal
carcinoma of the testis. The protein was also
found in tissue extracts of these 2 types of
tumors.

70-2135 THE ETIOLOGY, PATHOGENESIS AND
PROPHYLAXIS OF LEUKEMIAS IN HUMANS AND
ANIMALS IN THE LIGHT OF EPIDEMIOLOGIC STUDIES.
(E.) Aleksandrowicz, J. (3rd Clin. Intern. Dis.,
Cracow, Poland). Acta Med. Pol. 11(1):1-14,
1970. (96 references)

Studies involving genetic predisposition,
environmental factors (such as clustering,
association with aflatoxins, or exposure to
cattle with bovine leukosis), dietary effects
and viral etiology as they pertain to the
development, pathogenesis and treatment of
leukemia are reviewed, with particular reference
to epidemiological reports from Europe, especially
Poland.

70-2136 A REVIEW: PERINATAL-CONGENITAL
LEUKEMIA IN TWINS. (E.) Keith, L.,
E. Brown (Chicago Med. Sch., Ill.) and C. Fields.
Chicago Med. Sch. Quart. 29(1-2):1-8, 1970.
(43 references)

The high probability of leukemia developing
among twins, particularly monozygotic pairs, is
discussed in relation to other factors such as
exposure to ionizing radiation and viruses,
direct metastasis, chromosomal aberrations and a
conjoined intrauterine circulation. Cases of
15/62 pairs of twins in published reports of
leukemia in the perinatal-congenital (premature,
stillborn and 0-2 yr. old) age group are reviewed.

70-2137 EPIDEMIOLOGY OF CHILDHOOD NEOPLASIA.
Miller, R. W. Pp. 13-24 in Neoplasia
in Childhood. Year Book Medical Publishers,
Chicago, 1969, 336 pp. (44 references)

Clues to the etiology of various childhood
neoplasms were obtained by comparing patterns
of distribution and the incidence in subjects
with other diseases associated with a high risk;
these comparisons suggest that apparently un-
related tumors may have a common origin. Wilms'
tumor, adrenocortical neoplasms and primary
liver cancer are all associated with congenital
hemihypertrophy. Other neoplasms, which were
originally thought to have a common origin, were
shown to be etiologically distinct; for example,
genetic disorders associated with lymphoma are
not found in any form of leukemia except the
acute lymphocytic type and, conversely, children
who are at high risk for leukemia are not at
high risk for lymphoma.

70-2138 VIRUSES ASSOCIATED WITH BURKITT'S LYMPHOMA. Manaker, R. A. Pp. 455-459 in Biology of Amphibian Tumors, Mizell, M. (Ed.). Springer-Verlag, New York, 1969, 484 pp. (Recent Results Cancer Res., Special Suppl.). (26 references)

In studies of the association of viruses with Burkitt's lymphoma, it is concluded that reovirus Type 3 and the Epstein-Barr virus are frequently associated with the disease. Evidence includes the detection of the 2 viruses in pts. with Burkitt's lymphoma, in whom the viral agents are commonly transmitted by arthropod vectors, and in regions where some immunity to tumor development is suggested.

70-2139 ETIOLOGY OF MULTIPLE SCLEROSIS AND HODGKIN'S DISEASE. (E.) Newell, G. R. (NCI, Bethesda, Md.). Amer. J. Epidemiol. 91(2): 119-122, 1970. (22 references)

Evidence is presented to suggest several epidemiologic features common to multiple sclerosis (MS) and Hodgkin's disease (HD): similar patterns of geographical distribution (for young adults in the U.S.); low frequencies in Japan; clinical onset at about the age of 30 yr.; a tendency to occur in persons of high socio-economic status; and a definite, if low, familial occurrence (attributed to environmental, not genetic, factors). A female predominance is seen in the younger age groups, and a male predominance in older pts., with MS; in pts. with HD, a male preponderance is noted for all ages. Both diseases may develop after prolonged latent periods, following exposure to a carcinogenic factor early in life (at about the age of 15 for MS and at or before the age of 9 for HD). It is suggested that these 2 diseases may have a common etiology or may be related to common intermediate etiologic factors, perhaps 1 or more viruses. The possible role of a "slow" virus infection is mentioned.

70-2140 EFFECT OF SYNTHETIC INTERFERON INDUCERS ON MALIGNANT TUMORS AND VIRAL TUMORIGENESIS. (Rus.) Anonymous. Vop. Virus. 15(2): 247-249, 1970. (30 references)

Inhibition of tumor formation (induced by murine leukemia and sarcoma viruses and adenoviruses) by synthetic, 2-stranded RNA preparations which induce interferon synthesis is discussed. These included Statolon (obtained from the fermentation of Penicillium stoloniferum) and a complex of polyribonucleosinic and polyribocytidylic acids (Poly I:C). References are primarily to the American and British literature.

70-2141 With Special Reference to Tumor Immunity in the Primary Autochthonous Host. Immunology of Cancer, Takeda, K. Hokkaido University School of Medicine, Sapporo, 1969, 170 pp. (164 references)

Transplantation immunity against autochthonous tumors in primary hosts; cancer immunotherapy;

localization and nature of the tumor-specific antigen; the search for a cancer-specific antibody responsible for rejection phenomena; and general considerations of cancer immunity are discussed.

70-2142 VIRAL CARCINOGENESIS. (Bul.) Rangelova, S. Onkologiya 6(2):67-77, 1969. (98 references)

Viral-induced malignant transformation of cells in vitro, the role of DNA- and RNA-containing tumor viruses and defective and latent viruses in carcinogenesis, tumor antigens and evidence supporting the hypothesis that some human tumors are caused by viruses are presented.

70-2143 IMMUNOLOGICAL APPROACHES TO THE STUDY OF VIRAL ANTIGENS ASSOCIATED WITH NEOPLASMS. Gerber, P. Pp. 441-444 in Biology of Amphibian Tumors, Mizell, M. (Ed.). Springer-Verlag, New York, 1969, 484 pp. (Recent Results Cancer Res., Special Suppl.). (12 references)

Evidence demonstrating a virus-cell relationship in mammalian tumor cells, which is analogous in some respects to the lysogenic state in bacteria, is presented. Immunologically, tumors of higher vertebrates should be divided into 2 groups: tumors induced by DNA viruses, and tumors and leukemias induced by RNA viruses of the avian leukosis and murine leukemia complexes. It is concluded that the detection of specific antigens in virus-free tumors specified by the persisting viral genome provides a method of determining tumor etiology by immunological approaches.

70-2144 THE USE OF POLYOMA VIRUS FOR STUDIES ON GENETIC REGULATION IN MAMMALIAN CELLS. (E.) Weil, R. (Swiss Inst. Exp. Cancer Res., Lausanne) and R. Hancock. Bull. Schweiz. Akad. Med. Wiss. 25(1-2):35-45, 1970. (32 references)

The physicochemical and biological properties of DNA from mouse polyoma virus and the interaction of this virus with cultured mammalian cells are reviewed. It is concluded that circular polyoma DNA is a useful tool to study genetic regulation in mammalian cells because of its small size and its remarkable physical and biological stability.

70-2145 NUCLEIC ACID HOMOLGY AS APPLIED TO INVESTIGATIONS ON THE RELATIONSHIP OF VIRUSES TO NEOPLASTIC DISEASES. Green, M. Pp. 445-454 in Biology of Amphibian Tumors, Mizell, M. (Ed.). Springer-Verlag, New York, 1969, 484 pp. (Recent Results Cancer Res., Special Suppl.). (12 references)

Recent results of studies on adenovirus (AV)-transformed cells and AV-induced tumors of hamsters, rats and mice are discussed, in which molecular biology is applied to detect gene activity in AV-induced tumors and transformed cells, to investigate viral oncogenesis, and to analyze human tumors for AV genetic information. The application of nucleic acid homology procedures to the detection of virus-specific molecules in tumors is discussed.

-2146 BACKGROUND AND CURRENT STATUS OF THE SEARCH FOR ETIOLOGICAL AGENTS IN LEUKEMIA AND LYMPHOMA IN MAN. Rauscher, F. J., Jr. Pp. 25-49 in Neoplasia in Childhood. Year Book Medical Publishers, Chicago, 1969, 336 pp. (29 references)

Although all of the known viruses which produce leukemia and lymphoma in laboratory animals contain RNA, it is possible that the viruses which produce these diseases in man may not contain RNA. The possible role of Type C particles, mycoplasma, and herpes-type viruses is considered in studies of the etiology of human leukemia and lymphoma.

-2147 HERPES SIMPLEX VIRUSES AND HUMAN CANCER: CURRENT STATUS OF THE PROBLEM. Mizman, B. Pp. 478-481 in Biology of Amphibian Tumors, Mizell, M. (Ed.). Springer-Verlag, New York, 1969, 484 pp. (Recent Results Cancer Res., Special Suppl.). (33 references)

It is concluded that although there has been a long-standing association between herpes simplex virus (HSV) and cancer of the genitals and squamous carcinoma of the lip in man, sufficient evidence has not yet been gathered from experiments with carcinogenic viruses in experimental animals, thus still leaving doubt as to the oncogenicity of HSV.

-2148 PERSISTENT IMMUNOLOGIC STIMULATION AS A FACTOR IN ONCOGENESIS, WITH SPECIAL REFERENCE TO BURKITT'S TUMOR. (E.) O'Connor, T. (NCI, Bethesda, Md.). Amer. J. Med. 33(3):279-285, 1970. (65 references)

A hypothesis which relates the effect of persistent immunologic stimulation to the induction of Burkitt's lymphoma is based on a review of previous studies. The action of an infectious agent, which also has a transforming capacity, in an altered host is suggested.

-2149 A HERPES VIRUS AS A CAUSE OF MAREK'S DISEASE IN CHICKENS. Burmester, B. R., L. Witter, K. Nazerian and H. G. Purchase. Pp. 460-468 in Biology of Amphibian Tumors, Mizell, M. (Ed.). Springer-Verlag, New York,

1969, 484 pp. (Recent Results Cancer Res., Special Suppl.). (24 references)

Tissue culture studies in which an etiological agent of Marek's disease (MD) was identified are reviewed. This agent is cell-associated herpes virus isolated from chickens with MD.

70-2150 STUDIES ON THE VIRAL ETIOLOGY OF MAREK'S DISEASE OF FOWL. Richey, D. J. Pp. 469-477 in Biology of Amphibian Tumors, Mizell, M. (Ed.). Springer-Verlag, New York, 1969, 484 pp. (Recent Results Cancer Res., Special Suppl.). (34 references)

A general description is given of Type I and Type II (Marek's disease; MD) avian lymphoid leukosis. Body temperature of birds with MD is discussed as are various means of disease transmission. Cell-association of MD isolates and the release of the GA isolate from chick kidney cell culture are reviewed. Available information concerning the etiology of MD strongly suggests a herpes virus as the causative agent.

70-2151 CHROMOSOME ABNORMALITIES ASSOCIATED WITH CHRONIC LYMPHOID LEUKEMIA, MALIGNANT LYMPHORETICULAR PROCESS AND KAHLER'S DISEASE. (Fr.) Broustet, A. (Bordeaux CHU Cancer Ctr., France), C. Meuge and E. Legrand. Nouv. Rev. Franc. Hemat. 10(1):91-99, 1970. (10 references)

The cytogenetic anomalies of chronic lymphatic leukemia, Brill-Symmer's giant follicular lymphoma, Burkitt's lymphoma, lymphosarcoma, Hodgkin's disease, reticulum cell sarcoma, Waldenström's macroglobulinemia and IgG and IgA melanomas are described. Chromosomal variations were too great for any effective relationship to be seen. It is concluded that normal as well as abnormal chromosomes can be present in cases of malignant lymphatic diseases. Frequent chromosomal aberrations included pseudodiploidy and hyperploidy, especially in hematosarcomas. Further studies of WBC and bone marrow cells, as well as cells of many other organs, from lymphatic disease pts. are suggested.

70-2152 CHROMOSOME ANOMALIES IN ACUTE LEUKEMIA. (Fr.) Ruffié, J. (CNRS Blood Typing Ctr., Toulouse, France), J. Ducos, P. Colombies and E. Carles-Trochain. Nouv. Rev. Franc. Hemat. 10(1):84-91, 1970. (28 references)

Irregularity or lack of standard chromosome behavior in pts. with chronic or acute leukemia, or acute familial leukemia and leukemia in twins, is discussed in a survey of the literature since 1959.

70-2153 THE RELATIONSHIP BETWEEN PROGRESSIVE SCLERODERMA AND MALIGNANT TUMOURS.

(Ger.) Holzmann, H. (Univ. Derm. Clin., Mainz, Germany) and W. Frisch. Aerztl. Forsch. 24(5): 129-140, 1970. (89 references)

Bronchial carcinoma with a pleural effusion developed in 1/33 pts. (a 54-yr.-old woman) being treated for progressive scleroderma. Review of 98 previously reported cases, in which a malignant tumor developed in the presence of progressive scleroderma, concludes that there is no evidence of positive syntropy between the 2 disorders.

70-2154 ULTRASTRUCTURAL CHARACTERISTICS OF TUMOR CELLS. (Jap.) Ono, T. (Sapporo Med. Coll., Japan), Y. Fuse and M. Mori. Sapporo Igaku Zasshi (Sapporo Med. J.) 34(4):169-180, 1968. (27 references)

Ultrastructural characteristics of hepatomas induced by azo dyes (especially the 4-dimethyl-aminoazobenzene and 3'-methyl-4-dimethylamino-azobenzene "minimal deviation" rat hepatomas) are discussed. The most characteristic features were atypism of the cells and their cytoplasmic organelles, dedifferentiation and variability. The ultrastructural variability seemed to be the most prominent characteristic of these tumors, and was attributed to a "confusion" of differentiation. "Oval cell proliferation" played the most important role in the variability of azo dye-induced hepatomas.

70-2155 CHEMICAL CARCINOGENESIS, CHEMOTHERAPY: CANCER'S CONTINUING CORE CHALLENGES - G. H. A. CLOWES MEMORIAL LECTURE. (E.) Heidelberger, C. (U. Wisconsin Med. Sch. McArdle Lab. Cancer Res., Madison). Cancer Res. 30(6): 1549-1569, 1970. (143 references)

Interaction between chemical carcinogens, particularly 1,2:5,6-dibenzanthracene, and mouse skin proteins is discussed. Mouse skin h protein, suggested to be a repressor, forms covalent bonds

with carcinogenic, but not noncarcinogenic, hydrocarbons in vivo in direct relationship to their carcinogenic activities. In vitro studies of chemical carcinogens revealed that aneuploid cell lines derived from C3H mouse prostate underwent transformation when treated with 3-methylcholanthrene (MC) or other carcinogens. No evidence was found to indicate that MC acts selectively on pre-existing malignant cells or that it activates a latent virus. Possible relations between mutagenesis and carcinogenesis are considered.

70-2156 NITROGEN COMPOUNDS IN TOBACCO SMOKE. (Ger.) Neurath, G. (H. F. & P. F. Reemtsma, Hamburg, Germany). Arzneimittelforschung 19(7):1093-1106, 1969. (138 references)

It is emphasized that modern analytical methods have increased the number of known nitrogen compounds in tobacco smoke from about 50 in 1959 to 181 at time of the review. It is also suggested that the balance of all nitrogen compounds in tobacco smoke condensate indicates the existence of still other, as yet unknown, neutral nitrogen compounds.

70-2157 SKIN CARCINOGENESIS, MAMMALS VERSUS AMPHIBIA. Giovanella, B. C. Pp. 195-203 in Biology of Amphibian Tumors, Mizell, M. (Ed.). Springer-Verlag, New York, 1969. 484 pp. (Recent Results Cancer Res., Special Suppl.). (17 references)

It is suggested that the present definition of malignancy be revised upon consideration of results of experiments which showed that long-term cultures of highly malignant tumors (induced by 7,12-dimethylbenzanthracene), and s.c. transplants of these carcinomas in mice, became progressively less malignant. It was also demonstrated that hairless mice, although from a high-tumor strain, are completely resistant to skin carcinogenesis; this is attributed to a lack of hair follicles. Such results are compared to those for amphibia, which are similarly hairless and resistant to cutaneous carcinogenesis.

PHYSICAL CARCINOGENESIS

2158 SKIN CANCER AT THE SITE OF SCARS, FISTULAS AND ULCERS. (Rus.) Khazov, D. (I. P. Pavlov Med. Inst., Ryazan, USSR). Intn. Khir. 103(7):60-63, 1969.

460 pts. with cancerous diseases involving soft tissues of the trunk and extremities, (12 men and 4 women) had skin cancer which developed at the site of scars resulting from trauma or thermal burns (4 cases), long-standing fistulas associated with chronic osteomyelitis (4 cases), and trophic ulcers (6 cases). In 3 cases trophic ulcers were caused by varicose veins and in 3 others, by trauma associated with nerve damage and penetration of foreign bodies into soft tissue. Tumors were located on the trunk in 10 cases, on the hip in 4 and on the extremities in 2. The period of time from development of the skin lesion to development of cancer ranged from 8-35 yr. One illustrative case report is presented and the importance of histological diagnosis is stressed.

2159 VERRUCOUS SQUAMOUS CELL CARCINOMA OF THE ESOPHAGUS FOLLOWING LYE STRICTURE. (E.) Parkinson, A. T. (Berkshire Med. Ctr., Northampton, Mass.), G. L. Haidak and R. P. O'Connell. Chest 57(5):489-492, 1970.

67-yr.-old man presented with verrucous squamous cell carcinoma occurring at the site of stricture of the esophagus following ingestion of lye 31 yr. previously. The gross, histologic and behavioral characteristics of esophageal squamous carcinoma are similar to those of squamous carcinoma of the oral cavity, larynx, nasopharynx and vulva although the appearance of keratinized areas seems peculiar to esophageal squamous carcinoma. This tumor had been present for over 18 mo. but autopsy revealed no evidence of invasion of the muscular layers or the surrounding structures of the mediastinum, including lymph nodes, indicating a very slow growth. No metastases were found.

2160 CARCINOMA OF THE ESOPHAGUS ARISING IN PATIENTS WITH ACHALASIA OF THE CARDIA. (E.) Pierce, W. S. (U. Pennsylvania Hosp., Philadelphia, Pa.), H. MacVaugh, III and J. H. Johnson. J. Thorac. Cardiovasc. Surg. 59(3):331-339, 1970.

3/110 pts. with esophageal achalasia studied over a 15-yr. period, esophageal carcinoma developed after the achalasia symptoms had been present for an av. of 23 yr. The carcinoma was not advanced when detected. Malignant transformation is attributed to various factors such as chronic irritation of the mucosa by food and saliva, gastric secretions or the process of mechanical dilatation. It is suggested that carcinoma could be prevented by early elimination of esophageal stasis.

70-2161 ASPECTS OF CARCINOGENESIS IN SOLAR DAMAGED SKIN. (E.) Mitchell, R. E. (U. Tasmania, Hobart). Aust. J. Derm. 11(1):14-29, 1970.

A combined histological and electron microscopic study of premalignant conditions and of early and established malignant tumors (5 basal cell carcinomas, 1 squamous cell carcinoma, 4 lentigo maligna and 2 malignant melanomas) developing in solar damaged skin indicated that cells which are different from definitive cancer cells and also different from normal basal epidermal cells may be present at the periphery of tumors and may have features in common with basal cells in premalignant lesions. There were also changes in the basement membrane and in the superficial dermis which were peculiar to the individual lesion. The fine structure of the premalignant lesions was similar to that seen in the early stages of experimental skin carcinogenesis. It is suggested that cancers develop in solar damaged skin from a gradual, often multicentric, change in the epidermal cells.

70-2162 BASAL CELL EPITHELIOMA IN A THERMAL BURN SCAR. (E.) Kanto, I. (Mt. Sinai Sch. Med. City Hosp. Ctr. Elmhurst, New York, N. Y.), B. W. Berger and J. M. Wilentz. J. Occup. Med. 12(5):170-172, 1970.

A 60-yr.-old man who developed a basal cell carcinoma on the forearm, 8 yr. after suffering a burn by contact with a hot rivet, is described. No signs of recurrence were noted 7 mo. after surgical removal of the tumor. The pathophysiology and diagnosis of burn tumors and the cause-and-effect relationship between trauma and cancer are briefly considered.

70-2163 BASAL CELL NEVUS SYNDROME: A CASE REPORT WITH ASSOCIATED CARCINOMA OF THE MAXILLA. (E.) Shapiro, M. J. (St. Barnabas Med. Ctr., Livingston, N. J.). Laryngoscope 80(5):777-787, 1970.

Basal cell nevus (BCN) syndrome in conjunction with a spindle cell carcinoma of the maxilla is reported in a 55-yr.-old man who underwent radical surgery, but died within 6 mo. Pre-operative radiation therapy is suspected as possibly causing development of a highly malignant form of the maxillary carcinoma. A brother and son are reported as being similarly affected with BCN syndrome.

70-2164 THYMUS CELL POPULATION STUDIES DURING RADIATION LEUKEMOGENESIS. (E.) Fabrikant, J. I. (Johns Hopkins U. Sch. Hyg. Public Health, Baltimore, Md.). Amer. J. Roentgen. 108(4):729-735, 1970.

Male, 4-week-old C57BL/6J mice received X-irradiation (200 rads, 1 admin./week x 4 weeks). By 25 weeks, more than half had developed lymphomas, with the thymus being 3-fold the size of control organs. Study of reticular cells and small, medium and large lymphocytes of the thymus showed an over-all increase in the proportion of proliferating cells. At 25 weeks, about 30% of the lymphoma cell population became labeled with tritiated thymidines, indicating growth of medium and small lymphocytes. During development of lymphoma, the proportion of undifferentiated large lymphocytes increased as that of more mature cell populations decreased. A similar and significant failure to differentiate was noted during viral leukemogenesis in AKR mice in other studies. It is concluded that the increased duration of DNA synthesis and cell cycle time during lymphoma development, 2-fold at the time of dissemination, is due to polyploidy or aneuploidy, possibly as a result of breakdown of cellular control mechanisms.

- 70-2165 CYTOGENETIC STUDY ON LEUKEMIA IN ATOMIC BOMB SURVIVORS. (Jap.) Uchino, H. (Hiroshima U. Res. Inst. Nuclear Med. Biol., Japan). Nippon Ketsueki Gakkai Zasshi (Acta Haemat. Jap.) 31(5):818-824, 1968.

In 25 radiation-exposed pts. with chronic granulocytic leukemia (CGL; 11/25), CGL in acute transformation (1/25) or acute granulocytic leukemia (13/25), the frequencies and types of cytogenetic abnormalities seen in the leukemic cells were about the same as those noted in cells from 47 non-exposed pts. with the same diseases. In 1 radiation-exposed pt. with CGL, however, the Philadelphia (Ph¹) chromosome was detected in very high frequency, even in the very early stages of the disease. Physical and clinical laboratory findings in 11 exposed pts. with CGL suggested a milder course of the disease than in 11 non-exposed pts. with CGL.

- 70-2166 STATISTICAL SURVEY ON LEUKEMIA AMONG INDIVIDUALS IRRADIATED OCCUPATIONALLY AND THERAPEUTICALLY IN EAST JAPAN. (Jap.) Miyata, H. (Japan Red Cross Cent. Hosp., Tokyo), H. Enomoto and K. Maeda. Nippon Ketsueki Gakkai Zasshi (Acta Haemat. Jap.) 31(5):784-791, 1968.

In a statistical study of leukemia developing in individuals exposed to ionizing radiation in eastern Japan, 89 cases of leukemia that developed over a 20-yr. period were reported, including those occupationally-exposed, given radiotherapy for various diseases (X-irradiation and radioiodine therapy), given Thorotrast inj., children who had been exposed to X-irradiation in utero, atomic bomb survivors, and others who had been in Hiroshima and Nagasaki soon after the bombing. Most leukemias were myeloid, with chronic types occurring in the occupationally-exposed and acute forms developing after therapy (ratios of acute to chronic types were 0.8:1 and

5.8:1, resp., for the 2 groups). A-bomb-exposed pts. had an acute:chronic ratio of 0.9:1. A relationship between type of exposure and form of leukemia developed is suggested.

- 70-2167 LEUKEMIA IN RADIOLOGICAL WORKERS AND IN PATIENTS TREATED WITH IONIZING RADIATION (WEST JAPAN). (Jap.) Wakisaka, G. (Kyoto U. Int. Med., Japan) and S. Kariyone. Nippon Ketsueki Gakkai Zasshi (Acta Haemat. Jap.) 31(5):792-804, 1968.

The records for 1960-1967 of 500 hospitals in western Japan disclosed leukemia in 25 radiologists and physicians and in 28 pts. previously treated by radiotherapy. The av. latent periods in these 2 pt. groups were 11.4 and 3.9 yr., resp. No clear relationship between the latent period and the radiation dose was found. Relative proportions of acute and chronic myeloid leukemia in the physicians (44.0% and 40.0%, resp.) were significantly different from those seen in the radiation-treated pts. (28.0% and 56.0%, resp.; about the same as in all of Japan). In contrast to the relatively high prevalence of acute leukemia in the younger age groups in all of Japan, the pts. with radiation-induced acute or chronic leukemia showed a relatively homogeneous distribution between 20 and 60 yr. of age. Very few aleukemias were seen among the radiation-induced leukemias. Hematological pictures and clinical courses in the pts. with radiation-induced leukemia were similar to those with leukemia not induced by radiation.

- 70-2168 POSTOPERATIVE RADIOTHERAPY FOR BREAST CANCER AND LATE LEUKEMOGENESIS. (Jap.) Yamasaki, M. (Niigata U. Sch. Med., Japan), S. Kurokawa and T. Kitabatake. Nippon Igaku Hoshasen Gakkai Zasshi (Nippon Acta Radiol.) 29(1):44-48, 1969.

In a statistical study of the relationship between radiation therapy (RT) for breast carcinoma and resultant development of leukemia, 10 cases were found from 1953-1963 in women (age 40-59 yr.) who had received RT between 1941-1962. This value, greater than the expected number of 8 cases for an equivalent population, is considered statistically significant.

- 70-2169 AGE-DISTRIBUTION OF CANCERS CAUSED BY OBSTETRIC X-RAYS AND THEIR RELEVANCE TO CANCER LATENT PERIODS. (E.) Stewart, A. M. (Oxford U., England) and G. W. Kneale. Lancet 2(7662):4-8, 1970.

A comparison was made of the onset-age distributions of 5802 children who died of spontaneous or idiopathic cancers, and of 1045 children whose mothers had been X-irradiated during pregnancy and who later died of cancer. Only

Children who died before the age of 10 yr. were included. Cases were divided into 10 diagnostic groups corresponding to the anatomical positions of the primary tumor. Latent periods for radiogenic cancers varied with the type of cancer and varied continuous growth of the tumors from the time of irradiation. This comparison included 423 "extra" X-irradiated cases, 20 of which were ascribed to cerebral tumors diagnosed within a few weeks of birth after threatening to obstruct labor. For the other 403 cases, which were probably radiation-induced, the latent periods corresponded to the ages at the onset of symptoms. The ratios of spontaneous to radiogenic cancers was the same for hematopoietic and solid tumors (16.2:1 and 15.2:1, resp.); the range of ratios was no wider for groups containing distinct types of cancer than for groups containing several varieties. This suggests that whole-body irradiation does not tend to increase the incidence of any one type of cancer to the exclusion of others, when irradiation occurs in utero.

170 AUTOPSY CASE OF CARCINOMA OF THE BILE DUCT PRESUMABLY CAUSED BY THOROTRAST EMULSION. (Jap.) Yuda, K. (Chiba Nat. Univ., Japan), T. Nagashima, N. Yamazaki, A. Sukata and H. Kawakami. Iryo 23(2):241-246, 1969.

Autopsy of a 48-yr.-old male who had been administered thorotrast 25 yr. previously for splenography showed accumulation of Thorotrast in the liver, spleen and abdominal lymph nodes, a necrotic spleen, carcinoma of the bile duct, liver metastasis, adenocarcinoma of the cholecystic duct, peripapillary membrane, metastases to the peripapillary lymphatic tissue and an epithelial tumor of the esophagus.

171 EXPERIMENTAL LUNG CANCER IN RATS AFTER RADON INHALATION ASSOCIATED WITH EMULSION OF NONRADIOACTIVE DUST. (Fr.) Chameaud, R. (Atomic Energy Comm., Razes, France), Chameaud, R. Masse and J. Lafuma. C. R. Acad. Sci. [D] (Paris) 270(21):2594-2595, 1970.

Large tumors developed in 10/11 rats given a single inhalation of 1 mg of cerium hydroxide emulsion (0.2 mg of which was retained) followed by 108 sessions of exposure to 7.5×10^{-7} Ci/liter of radon (total dose delivered to the lung, 10 rads) over a 10-mo. period. Tumors began to develop during mo. 10 of the experiment. Autopsies, performed before mo. 15, showed 6 squamous cell carcinomas, 1 fibrosarcoma, 1 squamous cell carcinoma of the nostril with a small pulmonary lesion, and 2 cases of pulmonary adenomatosis. Tumors appeared to originate from the bronchioloalveolar epithelium or submucosa.

70-2172 THORIUM DIOXIDE ANGIOGRAPHY FOLLOWED BY BILE DUCT CARCINOMA; A CASE REPORT WITH RADIOLOGICAL STUDIES. (E.) Katayama, H. (Hosp. St. Raphael, New Haven, Conn.), S. Sawada, H. Yoshinaga and W. J. Russell. Nippon Igaku Hoshasen Gakkai Zasshi (Nippon Acta Radiol.) 29(5):481-490, 1969.

A 47-yr.-old Japanese male received thorium dioxide (TD) angiography 23 yr. prior to hospitalization due to increasingly severe, intermittent dull low back pain. He was found to have a mass in the epigastrium and enlarged left cervical lymph nodes. Cervical node biopsy revealed adenocarcinoma. Autopsy showed tumors or nodules in many parts of the body (cervical area, lungs, spleen) including a bile duct carcinoma originating in the right lobe of the liver. Radiography, autoradiography, spectroanalysis, chemical analysis, and scintillation counter studies demonstrated the presence of TD in liver, spleen and cervical tissue. A causal relation between TD and the neoplasms is suggested.

70-2173 RADIATION-INDUCED THYROID NEOPLASMS IN MAN. Hempelmann, L. H. Pp. 267-277 in Thyroid Neoplasia, Young, S. and D. R. Inman (Eds.). Academic Press, London, 1968, 470 pp.

A survey of about 3000 persons (Rochester series) who received X-ray treatment (especially with anterior and posterior (AP) port arrangements) in infancy and who subsequently developed thyroid tumors revealed a dose response with a substantial number of neoplasms occurring for the 100-300-rad dose range. The high number of neoplasms occurring in the AP-treated group seems to be related to relatively large thyroid doses in cases where the gland was usually in the primary X-ray beam. Frequency of neoplasms increased rapidly for the 10-19-yr. age group, and an increase in carcinomas preceded that for benign neoplasms. Carcinomas also developed earlier in males than females. It is suggested that the pathogenesis of thyroid neoplasms in man is compatible with a theory that radiation damage to cells is the initiating factor and thyroid stress (mainly during rapid growth) is the promoting, or secondary, factor.

70-2174 DAMAGING EFFECT OF X-IRRADIATION OF LESS THAN 1000 RADS ON GOITROGENIC CAPACITY OF RAT THYROID GLAND. Doniach, I. Pp. 259-265 in Thyroid Neoplasia, Young, S. and D. R. Inman (Eds.). Academic Press, London, 1968, 470 pp.

X-irradiation (less than 1000 rads) of rat thyroid failed to produce an effect on secretory function, and produced impairment of cell renewal, shrinkage of the gland with time, partial inhibition of goitrogenesis, carcinogenic summation with

goitrogens and tumor induction. It is also possible that these X-rays increased thyrotropic secretion and reduced the life span of acinar cells. Using a total of 347 rats, a direct correlation was found between X-irradiation dosage and percentage impairment of a response to a 4-week challenge (methylthiouracil or aminotriazole). X-ray doses (250, 500, 750 and 1000 rads) produced 84.3%, 62.3%, 49.4% and 24.7%, resp., impairment of goitrogenesis.

- 70-2175 A COMPARISON OF RADIOBIOLOGIC EFFECTS OF ^{131}I AND ^{125}I RESPECTIVELY ON THE RAT THYROID. Gross, J., M. Ben-Porath, A. Rosin and M. Bloch. Pp. 291-306 in Thyroid Neoplasia, Young, S. and D. R. Inman (Eds.). Academic Press, London, 1968, 470 pp.

Comparison of the effects of i.p. inj. of 100 and 500 μC of ^{125}I and ^{131}I on the rat thyroid concluded that ^{125}I has a more disturbing effect on the hormonal synthetic pattern than on the response mechanism to thyroid-stimulating hormone. When female albino rats were admin. ^{125}I or ^{131}I (25 μC) or ^{125}I (300 μC), thyroid examination at 502 days revealed that only the 25 μC ^{125}I -treated group had tumors. Small doses of ^{125}I caused a greater-than-normal response to a goitrogen in terms of increased thyroid wt. and cell number and increased demand for thyrotrophic hormone from the pituitary, as indicated by increased wt. An explanation is given to explain these findings on the basis of the difference in particle energies of the 2 isotopes. It is not recommended at this time that ^{125}I be used for routine diagnostic purposes in humans.

- 70-2176 LUNG TUMORS IN RATS AFTER INTRATRACHEAL INSTILLATION OF SOLUBLE PLUTONIUM 239 COMPOUNDS. (Rus.) Erokhin, R. A. (Biophys. Inst., Moscow), N. A. Koshurnikova, V. K. Lemberg, A. P. Nifatov and A. A. Puzyrev. Gig. Tr. Prof. Zabol. 13(5):61-63, 1969.

A soln. of plutonium nitrate (PN) in 0.01 N nitric acid (pH 2.0) and a soln. of sodium plutonyltriacetate (SPA) in water (pH 6.5) and 0.01 N nitric acid produced lung tumors when instilled intratracheally into male and female Wistar rats (140-160 g). Rats were given doses of 0.00042-1.0 μC PN or 1 μC of SPA. The percentage of rats with tumors and the percentage with cancer were directly proportional to the dose of radiation and the latent period was inversely proportional to the dose. Instillation of 0.00042-0.031 μC primarily produced lymphosarcomas while instillation of 0.048-1 μC primarily caused carcinomas in the lung. Squamous cell carcinomas generally developed against a background of alveolar and bronchial metaplasia and extensive pulmonary fibrosis. Only 4.5% of the rats with this form of cancer had metastases into the regional lymph nodes and kidneys. Pulmonary adenocarcinomas were more extensive

and metastasized more frequently (41.4%) into the regional lymph nodes, kidneys, pericardium, thymus and thyroid. Extensive hemangiosarcomas, which were found in a few animals (particularly among those given 0.1 μC), infiltrated into the mediastinum and, in 57%, metastasized into the heart, kidney and spleen. Adenomas, which were found in controls given instillations of nitric acid alone, were the most common benign tumor. However, it is considered that α -radiation from the plutonium is of more significance than nitric acid in the production of both pulmonary fibrosis and pulmonary carcinoma.

- 70-2177 EXTRAPULMONARY TUMORS IN RATS AFTER INTRATRACHEAL INSTILLATION OF SOLUBLE PLUTONIUM COMPOUNDS. (Rus.) Erokhin, R. A. (Biophys. Inst., Moscow), N. A. Koshurnikova, V. K. Lemberg, A. P. Nifatov and A. A. Puzyrev. Gig. Tr. Prof. Zabol. 13(10):33-35, 1969.

When instilled intratracheally, a soln. of plutonium nitrate (PN; pH 2.0) or a soln. of sodium plutonyl acetate (SPA; pH 6.5) produced both pulmonary and extrapulmonary tumors in male and female Wistar rats (140-160 g). Rats were given 0.00042-1 μC of PN or 1 μC of SPA. With increasing doses the percentage of animals with malignant neoplasms increased and the latent period decreased. Most of the extrapulmonary tumors involved the endocrine system, primarily the adrenals, because of hormonal imbalances produced by radiation. Since a considerable amount of the plutonium was cleared from the lungs by the ciliated epithelium and was excreted through the g.i. tract, malignant tumors were also found in the esophagus, stomach, duodenum and elsewhere in the g.i. tract. Frequency of osteosarcomas increased with increases in the total dose of ionizing radiation in the skeleton. It ranged from 1.57% in animals given doses of 51 rads to 13% in those given 880 rads. SPA produced more osteosarcomas than PN because the former is more soluble, and thus more readily absorbed from the lungs.

- 70-2178 SURVIVAL OF MICE UNDER DAILY GAMMA IRRADIATION: PROGRESS REPORT FOR INCIDENCE OF SOME TUMORS. (E.) Grahn, D. (Argonne Nat. Labs., Argonne, Ill.), G. A. Sacher, R. J. M. Fry, J. M. Rust, E. M. Cooke and E. Staffeldt. Argonne Nat. Labs. Ann. Rep. ANL-7535:74-76, 1968.

Histological examination of reticular, ovarian, pulmonary and hepatic tissues of 1125 mice (strains A/Jax, BALB/c, C57BL/6 and B6C1) exposed to γ -irradiation (0-56 R/day for the duration of life) showed a high frequency of thymus tumors early in life and with high dose rate. A rise in the number of reticular tissue tumors at 1.3 R/day (but late in life compared to thymus tumors), and a lower tumor frequency at 2.6 and 6 R/day, were seen. A significant rise in the

urrence of ovarian tumors was seen in the 1.3-
y group, with the exception of the A/Jax
in.

- 179 EFFECT OF ROTARY MOTION ON CARCINOGENESIS.
(Jap.) Suzuki, S. (Nagoya City U.
Med., Japan). Nagoya Shiritsu Daikagu
Kai Zasshi (J. Nagoya City Univ. Med. Ass.)
(J):1517-1558, 1969.

were admin. 3'-methyl-4-dimethylaminoazo-
ene (3MeDAB; 0.06% in the diet) and exposed
rotary motion for 30 min., or 1-2 hours/day.
or tumors developed in 18-23 weeks in 75% of
rats rotated 2 hours and in 58%, 33% and 25%
or 1 hour, 30 min. or no rotation, resp.
or wt. increased for all groups and was max.
2-hour treatment; body wt. increase was
t for the 2-hour group and greatest in cons.
s. The RBC count decreased as rotation time
eased. Figures of WBC count changes were
significant. It is concluded that rotary
on causes stress which stimulates function
the pituitary gland or adrenal cortex, thus,
noting tumor development.

- 180 EFFECT OF NOISE ON CARCINOGENESIS.
(Jap.) Watanabe, K. (Nagoya City U.
Med., Japan). Nagoya Shiritsu Daigaku
Kai Zasshi (J. Nagoya City Univ. Med. Ass.)
(J):851-878, 1968.

s (10 weeks old, 185 g) were admin. 3'-methyl-
methylaminoazobenzene (3MeDAB; 0.06%) and
n exposed to noise (in units of 95 or 75
n). Liver tumors developed after 14 weeks in
95-phon-treated animals, after 17 weeks in
se exposed to 75 phon and after 18 weeks in

rats treated with 3MeDAB alone. Tumors developed
in 66.7% of the animals in 12-20 weeks after 95-
phon treatment; values for 75-phon-exposed and
unexposed rats were 33.3% and 27.8%, resp. After
95 phon exposure, the RBC count decreased the
first 2 weeks and then remained constant; RBC
counts increased slightly for the other 2 groups.
Greatest WBC count increase was seen for 95 phon
treatment. It is suggested that noise stimulates
3MeDAB induction of tumors by affecting the pitu-
itary or adrenal glands; also, an effect of
noise on major bodily functions (involving liver,
stomach and blood) is suggested.

- 70-2181 STRESS AS AN ONCOGENIC FACTOR IN THYROID
EXPERIMENTAL CANCER. Milcu, S. M.
Pp. 307-315 in Thyroid Neoplasia, Young, S. and
D. R. Inman (Eds.). Academic Press, London,
1968, 470 pp.

Hemithyroidectomized (htx.) and non-htx. male
Wistar rats received methylthiouracil (MTU; 25
mg/day for alternating periods of 30 days treat-
ment with 30 days pause, up to 8-20 mo.) and a
third group of MTU-treated htx. rats received
alternating periods of stress (electric shock;
2 min./day in weekly alternating periods for 8
mo.). Results showed that stress due to electric
shock increased the number of animals developing
thyroid tumor to 50%, shortened the tumor latent
period, influenced the histological structure
and induced carcinosarcomas (compared with only
epithelial tumors in non-stressed rats). Thyroids
of stressed rats exhibited a 26.4% increase in
the total catecholamine content. Electrical
shock in rats grafted with Walker 256 carcinosarc-
omas increased developing tumor wt. by 45%. It is
concluded that electrical shock stress has an
aggravating effect on thyroid tumorigenesis.

also abstract nos: 2124,2125,2126,2127,2131,2132,2136,2184,2299,2301,2319,2355,2381,2529,2530,
2559,2580,2602,2603,2604,2635,2657

70-2182 EFFECT OF ACTINOMYCIN D ON VARIOUS STAGES OF CHEMICAL CARCINOGENESIS.

(Rus.) Pyleva, Z. A. (Inst. Nutr. Cancer Lab., Moscow). Pat. Fiziol. Eksp. Ter. 14(1):54-59, 1970.

Skin painting experiments were run on 320 non-inbred male mice and 1050 hybrid CBA x C57/BC female mice. When applied simultaneously with 3-methylcholanthrene (MC; 1 drop in 0.5% benzene soln., 1 admin./week), topical application of actinomycin D (AD; 5 µg/week in acetone) had no significant effect on carcinogenesis. AD tended to accelerate papilloma development and, when applied in weeks 1-5 of the experiment, it speeded up malignant transformation. When mice were inj. i.p. with AD (75 µg/kg body wt.), it slightly accelerated papilloma development only when inj. simultaneously with MC application. Malignant transformation was accelerated only when AD was inj. after papillomas first appeared. When mice were painted with a 1% benzene soln. of croton oil starting 4 weeks after MC admin., AD (3 doses of 75 µg/kg body wt.; i.p. on consecutive days) significantly accelerated papilloma formation if it was admin. 2 weeks after MC, but otherwise had no effect on the latent period for papilloma development. When AD (7.5 µg/kg body wt.) was inj. i.p., it significantly stimulated papilloma development only when 5 doses were admin. before MC. These findings indicate that the effect of AD on chemical carcinogenesis depends upon the dose employed and the stage of tumor development at which it is admin. Different doses of AD apparently have different modes of action.

70-2183 THE EFFECTS OF IMMUNOSUPPRESSION ON THE INDUCTION AND IMMUNOGENICITY OF

CHEMICALLY INDUCED SARCOMAS. (E.) Fisher, J. C. (U. Virginia Med. Ctr., Charlottesville), R. C. Davis and J. A. Mannick. Surgery 68(1): 150-157, 1970.

Effects of immunosuppression (antilymphocyte serum, ALS) on the induction and immunogenicity of 3-methylcholanthrene (MC; 0.2 ml of a 1% suspension)-induced sarcomas were studied using both short-term (5 doses s.c., 2 weeks before or after MC admin.) or long-term (3 doses/week x 6 weeks from day 0-45 or from day 45 until tumor appearance) immunosuppression in mice. Results of both series showed no significant alterations in rate of appearance or frequency of tumors compared to controls. Antigenicity testing of mouse sarcomas induced during ALS immunosuppression revealed that several tumors contained tumor-specific transplantation antigens (TSTA) of a strength comparable to that for normal hosts. A dose-dependent pattern of earlier and accelerated tumor growth (in comparison to controls) occurred for ALS-treated mice. ALS pretreatment blocked the recognition and response to TSTA.

70-2184 ASSESSMENT OF THE SIGNIFICANCE OF THE INTRAMITOCHONDRIAL DENSE BODY IN

CARCINOGENESIS. (E.) Tarin, D. (U. Leeds Sch. Med., England). J. Invest. Derm. 55(1):26-30, 1970.

From a study of the effects of chemical carcinogens, irritants, trauma and mammary tumor virus (MTV) on mouse skin, it is concluded that the intramitochondrial dense body is of no significance in carcinogenesis and probably represents a nonspecific epithelial response to mild injury. Since dense bodies are more commonly found in the more superficial layers of hyperplastic epidermis and in epithelium undergoing squamous metaplasia, they may play a role in keratinization under abnormal conditions. Ultrastructurally identical dense bodies were found in mouse epidermal cells after painting with 3-methylcholanthrene (MC; 0.3% in acetone), benzene or turpentine (50% in acetone), or after skin wounding. Intramitochondrial dense bodies were not seen in mouse mammary tumors induced by C3H MTV or MC, or in spontaneous mammary tumors of unknown etiology obtained from C57 females. Intramitochondrial dense bodies were occasionally found in the sebaceous cells of normal mouse skin, but these structures differed in appearance from those found in carcinogen- or irritant-treated skin, or in wounded skin.

70-2185 ANTIGENICITY OF CELLS DERIVED FROM MOUSE PROSTATE CELLS AFTER MALIGNANT

TRANSFORMATION IN VITRO BY CARCINOGENIC HYDROCARBONS. (E.) Mondal, S. (U. Wisconsin Med. Sch. McArdle Lab. Cancer Res., Madison), P. T. Iype, L. M. Griesbach and C. Heidelberger. Cancer Res. 30(6):1593-1597, 1970.

Clones derived from in vitro transformation of C3H mouse prostate cells with 3-methylcholanthrene, contained multiple and distinct transplantation antigens. The immunogenicity of 17 clones was tested in adult male C3H mice. Mice were immunized by s.c. inj. of individual clones and ligating the resulting fibrosarcomas so that they regressed. Cells of the same clone were inj. s.c., and the number of tumors produced by different doses of transformed cells was compared with the number induced in untreated controls. Of these clones, 11 were definitely antigenic and only 1 was nonantigenic. No cross-reactivity was found within 7 pairs of clones obtained from the same culture dish or within 3 clones derived from 3 different dishes.

70-2186 IN VIVO ELECTROMETRIC STUDY OF CARCINOGENIC HYDROCARBON INTERACTION

WITH MOUSE EPIDERMIS. (E.) Smolen, V. F. (Purdue U. Sch. Pharm. Sci., Lafayette, Ind.), D. E. Snyder and R. J. Erb. J. Pharm. Sci. 59(8):1093-1098, 1970.

An electrometric method was used to determine fixed-charge density of the epidermal mouse skin colloids (as a function of pH) 1, 4, 9, 20, 34 and 50 hours after skin painting with a 1% wt./vol. soln. of 3-methylcholanthrene (MC) in benzene. Control mice were painted with benzene alone or were untreated. MC consistently reduced the net cationic fixed-charge density attributable to the loss or discharge of basic nitrogenous groups titratable above pH 7.4. These basic groups could include the guanidyl group of arginine, the ϵ -amino group of lysine, α -amino acid groups and some of the nitrogenous groups of purine and pyrimidine bases. It is suggested that MC might reduce the cationic charge density by an allosteric mechanism in which release of protons from affected macromolecular structures could result from interaction of MC at a few cardinal sites which control the acid-base properties of relatively large numbers of proton-binding sites. Such hydrocarbon-induced reductions of cationic charge density on nuclear proteins could conceivably derepress genes. This hypothesis is also capable of integrating various theories of carcinogenesis.

70-2187 DEVELOPMENT OF TUMOR IN TRANSPLANTED LUNGS OF NEWBORN AND ADULT MICE. (E.) Kimura, I. (Aichi Cancer Ctr. Res. Inst., Nagoya, Japan), T. Miyake and Y. Ito. Proc. Soc. Exp. Biol. Med. 134(2):504-506, 1970.

A/Jax mice of both sexes were treated with 3-methylcholanthrene (MC; single i.p. inj. of 0.2 mg in olive oil) following s.c. transplantation of newborn or adult mouse lung. At autopsy (15 weeks after transplantation), the number of tumors in the lung transplants was significantly higher in transplants derived from the newborn mice than in those obtained from adult mice. Histologically, the tumors were identical to spontaneous or MC-induced primary lung tumors. It is concluded that the age factor which influences tumorigenic responses of the lung to MC is located in the lung of the mouse itself.

70-2188 PULMONARY TUMOUR INDUCTION IN VITRO. GENETIC INFLUENCE. (E.) Flaks, A. (Leeds Sch. Med., England). Europ. J. Cancer 6(3):259-260, 1970.

Lung tissue from 1-mo.-old female mice of the lung tumor-resistant C57BL strain, was incubated with 3-methylcholanthrene (MC; 4 μ g/ml medium) in vitro. Other mice then received s.c. implants of the incubated lung tissue and were examined after 3, 6, 9 and 12 mo. for tumor development. MC-exposed tissue implants showed lymphocytic hyperplasia and some fibrosis, but no tumors developed at any time. The absence of tumor induction in vitro suggested that tissue-specific

genetic factors exercised a dominant role in the activity of MC on tissues from these resistant mice.

70-2189 HISTOPATHOLOGIC STUDIES OF EXPERIMENTAL GLIOMAS. HISTOCHEMICAL OBSERVATIONS AND TISSUE CULTURE OF THE TRANSPLANTS. (Jap.) Kawarai, M. (Gunma U. Sch. Med., Maebashi, Japan). Kitakanto Igaku (Kitakanto Med. J.) 19(1):1-25, 1969.

Admin. of 3-methylcholanthrene to a group of 84 C57BL mice by intracerebral inoc. produced gliomas, sarcomas and an epidermoid tumor in 6, 19 and 1 case, resp. The gliomas were successfully transplanted s.c. to other mice of the same strain; during serial transfer, the gliomas lost their polymorphism and showed strong enzyme activity. Dehydrogenase activity of gliomas was stronger than for sarcomas. In tissue culture, 2.6 gliomas showed marked cellular polymorphism.

70-2190 STUDIES ON A RECURRENCE OF TUMORS. I. RECURRENCE OF METHYLCHOLANTHRENE-INDUCED TUMORS IN RATS. (Jap.) Irino, H. (Gifu U. Sch. Med., Japan). Gifu Ikadaigaku Kiyo (Acta Sch. Med. Gifu) 16(4-5):623-635, 1969.

Male Donryu rats (90 g) were inj. with 3-methylcholanthrene (s.c. on the back) and developing tumors were partially or completely excised. The inj./excision cycle and regrowth of tumors was continued, and a study was made of effective i.p. transplantability. Tumors recurred in all animals; their growth rates were generally accelerated after excision. Repeated excision increased i.p. transplantability of tumors. No conversion to ascites tumors was seen.

70-2191 HISTOLOGICAL STUDY OF FORMATION OF MALIGNANCIES IN MICE BY 20-METHYLCHOLANTHRENE. (Jap.) Miura, M. (Nippon Med. Sch., Tokyo). Nippon Ika Daig. Z. 36(5):396-411, 1969.

Tumors were induced in 200 mice by inj. of 3-methylcholanthrene (0.5% in a 0.2 ml olive oil soln.). Carcinomas resulted in 83.3% and sarcomas in 44.4% (concurrently in 27.7% of the animals). Sarcomas infiltrated the muscular coat of the stomach, striated muscles and the skin. In the latter, it invaded the epidermis and hair follicles. No long-term metastases were noted after 16 weeks.

70-2192 EFFECT OF CENTRAL NERVOUS SYSTEM AGENTS ON TUMOR INDUCTION IN RATS. (Ger.) von Metzler, A. (Res. Inst. Fortified Milk, Frankfurt a. M., Germany). Klin. Wschr. 48(11):693-694, 1970.

Mean survival times in male and female BD 11 and Wistar rats, inj. s.c. with 3-methylcholanthrene (3 mg in a 1% suspension), were increased 2-3 fold when animals were treated with combinations of endotoxin from *Salmonella abortus equi* and ether, aluminum-dextran and ether, or endotoxin and short-wave irradiation of the head. Treatment was begun after tumor nodules became evident. Endotoxin (60-80 µg/100g or 20-30 µg/100g, depending upon the effectiveness of the preparation) was inj. into the jugular vein and was followed, 18-24 hours later, by s.c. inj. of 100 µg and 50 µg into males and females, resp. Rats were exposed to ether until they developed signs of central nervous system excitation. Aluminum-dextran (0.2 ml/100 g) was inj. into the jugular vein. The heads of rats were irradiated with short-waves for 3 min. (5 admin./week). None of these agents increased survival time when admin. alone. Survival times were shortened by treatment with endotoxin and camphor (0.2 ml of a 20% soln. 5 admin./week) or by endotoxin and quinine (1 ml of a 3% quinine hydrochloride soln. weekly, route unspecified).

70-2193 EFFECT OF 3-METHYLCHOLANTHRENE ON GOLDBLATT HYPERTENSION IN RATS. (Ger.) von Metzler, A. (Res. Inst. Fortified Milk, Frankfurt a. M., Germany). *Klin. Wschr.* 48(11): 694-695, 1970.

In female Wistar rats, inj. of 3-methylcholanthrene (MC; 3 mg in a 1% suspension) caused severe damage to the vasomotor center. Hypertension developed in only 3/55 rats given MC 10 days after unilateral nephrectomy and ligation of the renal artery on the opposite side. Blood pressure values were very low in some cases, particularly in animals with tumors, but abnormally low blood pressures were also noted in MC-treated rats without tumors. The survival time of operated MC-treated rats with tumors was somewhat longer than that of non-operated MC-treated rats with tumors, possibly because of the somewhat higher blood pressure values in the former group.

70-2194 EFFECT OF DEOXYCORTICOSTERONE ON BLOOD PRESSURE IN RATS AFTER PRETREATMENT WITH 3-METHYLCHOLANTHRENE. (Ger.) von Metzler, A. (Res. Inst. Fortified Milk, Frankfurt a. M., Germany). *Klin. Wschr.* 49(11):695-696, 1970.

Admin. of 3-methylcholanthrene (MC; 3 mg in a 1% suspension, s.c.) reduced blood pressure in male and female BD 11 rats. When depot deoxycorticosterone was admin. (DOC; 2 inj./week s.c. of 5 mg/100g, beginning 6 weeks after MC inj.) to unilaterally nephrectomized rats, blood pressure increased, tumor growth was inhibited, and survival times increased. Although the percentage of males with tumors was the same in DOC-treated

and untreated groups, only 3/11 males had large tumors; in 1 male the tumor regressed completely. The percentage of females with tumors was reduced from 50% to 10%.

70-2195 EFFECT OF CHLORTETRACYCLINE ON CARCINOGENESIS. (Rus.) Pyleva, Z. A. (Sci. Res. Inst. Nutr., Moscow). *Vop. Pitan.* 29(1): 71-77, 1970.

An 0.5% benzene soln. of 3-methylcholanthrene (MC) was applied to the skin of male noninbred mice at a rate of 1 drop/week. The latent period for papilloma development was reduced significantly when chlortetracycline (CTC; 15 mg/kg/day s.c.) was inj. for 7 consecutive days before or concurrently with MC application. The same dose of CTC had no effect on papilloma development when it was inj. 1 or 5 weeks after the first application of MC or at the first sign of papillomas. No effect on papilloma development was noted when CTC (50 mg/kg/day s.c.) was inj. for 10 consecutive days before MC application, concurrently with it, or 1 week after the first application. In another test, mouse skin was painted with a single dose of 2 drops of a 0.5% benzene soln. of MC. Four weeks later the same skin area was painted with a 1% benzene soln. of croton oil once a week. When CTC (15mg/kg s.c.) was inj. concurrently with MC application, the percentage of mice that developed papillomas and the number of papillomas/mouse increased significantly. The latent period for papilloma development was only slightly shortened. No significant differences were observed between experimental animals and controls when the same dose of CTC was inj. s.c. for 10 days before MC application, or 1 week after MC application. Even though the conditions used in these experiments are not the same as those under which CTC is used in practice, the tumor-promoting activity of this antibiotic should be remembered when considering its suitability for preserving food products.

70-2196 IMMUNOLOGIC STATUS OF HOST AND RESPONSE OF A METHYLCHOLANTHRENE-INDUCED SARCOMA TO LOCAL X-IRRADIATION. (E.) Suit, H. D. (U. Texas M. D. Anderson Hosp. Tumor Inst., Houston) and A. Kastelan. *Cancer* 26(1):232-238, 1970.

A fibrosarcoma, induced in a young C3H/He mouse by inj. of 3-methylcholanthrene (1 mg in peanut oil soln., s.c.) was studied to determine the number of tumor cells needed to transplant the tumor into half of the recipients (TD₅₀) and the dose of radiation required to achieve local control of half of the irradiated tumors (TCD₅₀). Recipients were male and female C3H/He and (C3H/He x C57BL)F₁ mice, aged 10-12 weeks. The TD₅₀ was 100-fold greater for recipients which had been actively immunized with 2 s.c. and 1 i.p. inj. of 2 x 10⁷ lethally irradiated tumor cells, than in immunologically depressed recipients

Given 400 rads of whole-body X-irradiation 24 hours before inoc. of the tumor cells. TCD₅₀ values were 4300 rads, 3500 rads, and 2700 rads for tumors transplanted into immunologically depressed mice, normal mice and actively immunized mice, resp. Immunization, started 7 or 14 days after irradiation of an established tumor, or whole-body irradiation, given 0 or 7 days after local tumor irradiation, had no effect on the TCD₅₀. This suggests that the primary immune response was fully developed by the time the tumor had grown to a volume of 250 mm³. Exposure of the thigh to 3500 rads X-irradiation 24 hours before challenge slightly delayed the appearance of tumors and slightly reduced the TD₅₀.

0-2197 EFFECT OF CASTRATION ON THE INDUCTION OF EPIDERMAL NEOPLASMS IN MALE MICE BY TOPICAL METHYLCHOLANTHRENE. (E.) Zackheim, J. S. (Stanford U. Sch. Med., Palo Alto, Calif.). *Invest. Derm.* 54(6):479-482, 1970.

Early papules and squamous cell carcinomas developed on the skin of 50 sham-operated controls and 48 orchiectomized (orx.) male Swiss mice after weekly applications of 3-methylcholanthrene (0.2 ml of a 0.3% soln. in benzene 16 weeks). Orx. at age 8 weeks reduced the median neoplastic surface area, the number of mice developing papules 2 mm or larger in diameter and the mean number of tumors per mouse. The only significant reductions, however, occurred in the number of mice developing papules at about 15-16 weeks. Results of these experiments support the hypothesis that testosterone may be a promoting factor for the development of epidermal neoplasms in response to topical application of carcinogens.

0-2198 EXPERIMENTAL BONE SARCOMAS INDUCED IN RATS BY VARIOUS CHEMICAL CARCINOGENS. (Jap.) Kurihara, T. (Nihon U. Sch. Med., Japan). *Nihon U. J. Med.* 27(9):921-941, 1969.

Wistar rats were inj. with 3,4-benzpyrene (BP), 3-methylcholanthrene (MC) and 4-nitroquinoline-oxide (NQO) into the bone marrow of the tibia. A total of 163 rats, sarcomas (no metastases) were induced in 8 admin. 1 mg BP, 10 receiving 1 mg BP, 15 given 6 mg MC, and in 2 and 10 rats admin. 1 and 6 mg NQO, resp. Greatest frequency of tumors (36%) was seen for MC-treated rats, and the shortest period of tumor development (20 weeks) was for those admin. 6 mg NQO.

0-2199 LUNG TUMORS IN MICE RESULTING FROM INTRAVENOUS INJECTION OF 20-METHYLCHOLANTHRENE AND 3,4-BENZPYRENE. (Bul.) Ivanov, I. (Sci. Res. Oncol. Inst., Sofia, Bulgaria). *Onkologija* 6(3):100-109, 1969.

Multiple pulmonary adenomas developed after 3-mo. in male and female CC57W mice were inj. i.v.

with 3-methylcholanthrene (MC; 2.5 and 1.25 mg) or 3,4-benzpyrene (BP; 1.25 mg) in a suspension with dextran and physiological saline. Adenomas developed in 100% of the mice 1-5 mo. after inj. of MC and in 66% of the mice 14-17 mo. after inj. of BP. MC induced an av. of 23 lung tumors/mouse while BP induced an av. of 16/mouse. MCA produced more subpleural adenomas than did BP. Tumor size and the number of tumors generally increased with the length of the induction period. No sex differences were noted in tumor development except for a slightly shorter latent period in females; this was more pronounced after BP inj. Histologically, the tumors found in MC- and BP-treated mice were the same as those found in 2/57 dextran-treated and untreated controls. Adenomas were trabecular, glandular-papillary or localized in structure, with few signs of malignant transformation. Capsules and infiltrative growth were absent, nuclear atypism was not very pronounced and only a slight increase in mitotic activity was seen.

70-2200 OSTEOSARCOMA INDUCED BY 3,4-BENZPYRENE. (Slovak) Kalman, E. (Comenius U. Fac. Med. Orthop. Clin., Bratislava, Czechoslovakia). *Acta Chir. Orthop. Traumat. Cech.* 36(1):4-11, 1969.

Studies on albino rats (initial wt. of 190 g) showed that implantation of sticks containing 3,4-benzpyrene (BP; 7 mg) and paraffin (14 mg) into the distal metaphysis of the left femur produced polymorphocellular sarcomas histologically identical to those found in man. A preliminary study on 25 rats showed that the latent period was 6 mo. The optimum dose of BP was 7 mg, because it did not cause local necrosis, but consistently induced sarcomas. Smaller doses of BP increased the latent period by 1 mo. and gave lower tumor yields. A study was made with 75 albino rats divided into 4 groups: 1) 7 mg BP implanted as described above; 2) 7 mg BP + 14 mg paraffin; 3) 10 mg pure paraffin; and 4) sham operation. Sarcomas developed in 15/20 group 1 rats, in 16/30 group 2 rats, in 0/15 group 3 rats and in 0/10 group 4 rats; 6 rats died of unrelated causes. No metastases were found in X-rays or on autopsy.

70-2201 DISTRIBUTION AND EXCRETION OF ³H-BENZ(α)PYRENE FROM THE ANIMAL BODY AFTER INTRATRACHEAL INSTILLATION WITH ASBESTOS AND CARBON BLACK. (Rus.) Pylev, L. N. (Inst. Exp. Clin. Oncol., Moscow), F. Roe and D. Vorvik. *Vop. Onkol.* 16(3):61-69, 1970.

Experiments were performed on a total of 243 golden hamsters given intratracheal instillations of ³H-3,4-benzpyrene (BP; 5 mg), 5 mg BP + 1 mg crocidolite asbestos (CA), and 5 mg BP + 1 mg carbon black in which 90% of the particles had diameters ranging from 26-160 μm. In all cases 0.2 ml of Aminosol Vitrum, to which small quantities of Tween 80 had been added, was used as the solvent. Radioactivity measurements

made on the lungs revealed a rapid clearance of BP from the lungs for the first 2 weeks, which did not differ significantly between the 3 groups. About 99% of the radioactivity disappeared during this period. Within 21 days after instillation, animals admin. BP + CA or BP + carbon black had significantly higher radioactivity values than those admin. only BP, due to retention of BP adsorbed on asbestos and carbon black. Radioactivity in the liver and kidneys reached a max. in all groups 24 hours after instillation. No differences were noted between the groups until late in the experiment, when hamsters treated with pure BP showed significantly lower values. Both urinary and fecal radioactivity became significantly lower in animals admin. BP + carbon black 36 days after instillation of BP. About 10-fold more radioactivity was excreted in the feces than in the urine. Pulmonary inflammation and exudation was most pronounced in hamsters admin. both BP and CA.

70-2202 IN VITRO METABOLISM OF BENZ(α)PYRENE BY CELLS FROM VARIOUS MAMMALIAN SPECIES AND THE TOXIC EFFECT OF POLYCYCLIC HYDROCARBONS ON THESE CELLS. (Rus.) Belitskii, G. A. (Inst. Exp. Clin. Oncol., Moscow), Iu. M. Vasil'ev, O. Iu. Ivanova, N. A. Lavrova, E. L. Prigozhina, N. L. Samoilina, A. A. Stavrovskaja, A. Ia. Khesina and L. M. Shabad. Vop. Onkol. 16(2): 53-58, 1970.

From a study of 3,4-benzpyrene (BP; 0.1 μ g/ml) and 7,12-dimethylbenzanthracene (DMBA; 1 μ g/ml) in embryonic fibroblast cultures of various species of mammals, it is concluded that the toxic effect of these carcinogens is related to the rate at which they are metabolized. BP and DMBA had a toxic effect on fibroblast cultures from embryonic rats and, to a lesser extent, on those from embryonic cats and guinea pigs. This toxic effect was due to a decrease in the number of cells synthesizing DNA. Neither BP nor DMBA had a toxic effect on embryonic human fibroblasts. BP was metabolized most rapidly by fibroblasts from embryonic mice, hamsters and rats, followed by those from guinea pigs and cats. Human fibroblasts metabolized BP more slowly than did fibroblasts from other species, but after 72 hours of incubation, human fibroblasts had metabolized 50% of the BP. The percentage of BP metabolized by WBC cultures from human adults was generally higher in cultures to which phytohemagglutinins had been added. However, there was considerable variation in the percentage of BP metabolized. This variation did not appear to be related to individual differences between donors.

70-2203 PHOTSENSITIZING EFFECTS OF AROMATIC HYDROCARBONS AND QUINOLINES UPON DNA. (E.) Kodama, M. (U. Wisconsin, Madison) and C. Nagata. Chem. Biol. Interactions 1(1): 99-112, 1969/70.

Photosensitizing effects of aromatic hydrocarbons, carcinogenic quinoline derivatives and aromatic amines on DNA were studied. Visible light photoirradiation of all but the aromatic amines gave a photosensitizing effect on DNA. Binding of 3,4-benzpyrene to the guanine residue of DNA, as well as the binding of 3,4-benzpyrenequinone, 3-methylcholanthrene and 7,12-dimethylbenzanthracene, was also seen during irradiation, but a correlation of the 2 phenomena could not be necessarily concluded.

70-2204 A COMPARATIVE STUDY OF THE EFFECTS OF PHENOBARBITAL AND 3,4-BENZPYRENE ON THE HYDROXYLATING ENZYME SYSTEM OF RAT-LIVER MICROSOMES. (E.) Gnosspelius, Y. (U. Stockholm), H. Thor and S. Orrenius. Chem. Biol. Interactions 1(2):125-137, 1969/70.

Studies on the hydroxylating enzyme system of liver microsomes obtained from male Sprague-Dawley rats showed that 3,4-benzpyrene (BP; 20 mg/kg i.p.) caused moderate increase of cytochrome P-450 absorption, no change in reduced nicotinamide adenine dinucleotide phosphate (NADPH)-cytochrome c reductase, and an increased hydroxylation rate with a small number of substrates, including primarily the polycyclic hydrocarbons. When added to the assay system in vitro, both BP and aminopyrine (AP) enhanced the initial rate of NADPH-cytochrome P-450 reduction; the stimulatory effect of BP was more pronounced in liver microsomes from BP-treated rats. Results suggest that in contrast to phenobarbital, BP yields a modified cytochrome (P-448) in the liver microsomes with an increased affinity for BP as well as a decreased affinity for AP.

70-2205 BENZO(α)PYRENE-METABOLIZING ENZYME ACTIVITY OF LIVERS OF VARIOUS STRAINS OF MICE. (E.) Kodama, Y. (Kyushu U., Fukuoka, Japan) and F. G. Bock. Cancer Res. 30(6): 1846-1849, 1970.

Liver homogenates from 6 different mouse strains were assayed for their 3,4-benzpyrene (BP) hydroxylase activities. BP hydroxylase activity was highest in liver homogenates from C57BL/6Ha mice and lowest in those from the DBA/2 strain; the activity of the former was 2-3-fold higher than that of the latter strain. The F₁ hybrids of C57BL/6Ha and C3H/StHa mice had BP hydroxylase activities similar to those of the C3H parent. The BP hydroxylase activity was somewhat higher in females than in males, but this difference was significant only in the DBA/2 strain. The amount of BP quinone formed in vivo by super-natants was also highest in C57BL/6Ha mice. After i.p. inj. of 0.3 mg BP in male mice, BP hydroxylase induction was very pronounced in the C57BL/6Ha and C3H/StHa strains and in their F₁ hybrid, but no induction was observed in DBA/2, A/St or Ha/ICR Swiss mice.

0-2206 CHEMICAL LINKAGE OF POLYCYCLIC HYDROCARBONS TO DEOXYRIBONUCLEIC ACIDS AND POLYNUCLEOTIDES IN AQUEOUS SOLUTION AND IN A BUFFER-ETHANOL SOLVENT SYSTEM. (E.) Hoffmann, J. D. (Johns Hopkins U., Baltimore, Md.), S. A. Lesko, Jr. and P. O. P. Ts'o. Biochemistry (Wash.) 9(13):2594-2604, 1970.

The results of a study of the iodine-induced reaction between 3,4-benzpyrene (BP) and DNA or ribosyl homopolynucleotides (RHPN) support the hypothesis that a BP radical cation is the active intermediate and indicate that the active intermediate in the iodine-induced reaction is probably different from that in the hydrogen peroxide-ferrous ion system. In reacting BP with DNA from calf thymus or *Bacillus subtilis*, a 10-100-fold increase in yield was obtained by performing the reaction in a solvent consisting of a 2:1 ratio of 10^{-2} M phosphate buffer (pH 6.8) and ethanol. In this solvent the iodine and hydrocarbon are more soluble and the DNA is less soluble than in an aqueous system. The yield can be further increased by stepwise addition of BP and by repeating the reaction after isolating the BP-DNA adduct. Under identical conditions carcinogenic hydrocarbons (BP, 7,12-dimethylbenzanthracene, and 3-methylcholanthrene) were 10-14-fold more reactive than their noncarcinogenic isomers or analogs (1,2-benzpyrene and 1,2-benzanthracene). Reactions of BP with various RHPN and their complexes indicate that BP is linked primarily to polyguanosine, even in the polyguanosine-polycytosine complex, in the iodine-induced reaction. Degradation of the BP-polyguanosine adduct to mononucleotides and examination by density gradient electrophoresis revealed that BP is linked preferentially to uridine polynucleotides, with polyguanosine being the most reactive, in a hydrogen peroxide-ferrous ion system.

0-2207 STUDY OF A YEAST GROWN ON DIESEL OIL IN THE PRESENCE OF 3,4-BENZPYRENE. (Cz.) Jula, J. (U. Nemochice 5, Prague), H. Bendová, V. Prágl and E. Drechslerová. Cas. Lek. Cesk. 99(6-7):158-162, 1970.

Chemical analysis showed no 3,4-benzpyrene (BP) in solid phases of extracts from yeasts grown on diesel oil. Solid phases contained aliphatic hydrocarbons with chains ranging in length from 7-24 carbons (C) atoms. Liquid phases contained saturated aliphatic hydrocarbons with chains consisting of 12-20 C atoms; mono-, di- and trialkylbenzenes with side chains having more than 2 C atoms; condensed and noncondensed cycloalkanes, indanes, tetralenes, alkylnaphthalenes, acenaphthenes, diphenyls, benzthiophenes and traces of polycyclic hydrocarbons with 3 rings. Similar analysis of yeasts grown on n-alkanes failed to show any presence of BP.

-2208 3,4-BENZPYRENE CONTENT IN SMOKED FISH TREATED WITH GAS COMBUSTION PRODUCTS.

(Rus.) Dikun, P. P. (N. N. Petrov Sci. Res. Inst. Oncol., Leningrad, USSR), N. D. Krasnitskaia, I. A. Shendrikova, O. P. Gretskaia, A. V. Emshanova and I. I. Lapshin. Vop. Onkol. 15(4):79-82, 1969.

The 3,4-benzpyrene (BP) content of 2 samples of codfish heat-cured in wood smoke (WS) was 2.9 and 4.2 $\mu\text{g/kg}$, resp. When codfish were cured with cold smoke from wood shavings and hot gas combustion products (GCP), values were 0.71 and 1.15 $\mu\text{g/kg}$, resp.; for GCP alone they were 0.46 and 0.22 $\mu\text{g/kg}$, resp. The BP content of bass cured with WS (3 samples) varied from 3.1-5.7; with curing fluid (CF) and GCP (4 samples) it varied from 0.23-0.44; with GCP alone (2 samples) values were 0.24 and 0.37, resp. Infrared radiation (IR) resulted in no BP detectable in 2 samples. The BP content in mackerel treated with CF and GCP was 0.15 $\mu\text{g/kg}$; CF + IR resulted in 0.05 $\mu\text{g/kg}$ and no BP was detected after IR treatment alone.

70-2209 REDUCING THE CONTENT OF POLYCYCLIC HYDROCARBON CARCINOGENS IN SMOKED FOOD PRODUCTS. (Rus.) Dikun, P. P. (N. N. Petrov Sci. Res. Inst. Oncol., Leningrad, USSR), N. D. Krasnitskaia, V. A. Lipova, I. A. Shendrikova, O. P. Gretskaia and A. V. Emshanova. Vop. Pitan. 28(3):81-85, 1969.

From studies of the 3,4-benzpyrene (BP) content of fish smoked by a variety of methods, it is concluded that the BP content can be reduced by lowering the temperature at which smoke is generated, replacing wood with sawdust or by filtering the smoke. The BP content of 6 fish samples cured in the Far Eastern rotary smoke oven ranged from 0.6-6.3 $\mu\text{g/kg}$ and the BP content of 4 fish samples cured in the Murmansk vertical smoke oven ranged from 1.3-2.3 $\mu\text{g/kg}$. These values are about the same as the BP content of fish cured conventionally with hot smoke. The Far Eastern oven uses wood and the Murmansk oven both wood and sawdust as fuel. The BP content of 4 herring samples smoked in a modern tunnel oven ranged from 0.10-0.25 $\mu\text{g/kg}$. This oven uses both wood and wood shavings as fuel for low-temperature curing. The BP content of 6 fish samples cured in a smoke generator for low-temperature curing ranged from 0-0.19 $\mu\text{g/kg}$. No BP at all was found in herring cured in the smoke generator but 0.01-0.35 $\mu\text{g/kg}$ were present in *Clupeonella*, probably because of the large difference in the size of these fish. Similar results were obtained with a smoke generator in which the smoke was passed through a resin and filtered before the fish were exposed to it. The BP content in fish cured by this method ranged from 0-3.6 $\mu\text{g/kg}$.

70-2210 STUDY OF BENZPYRENE CONTENT OF SODIUM CHLORIDE SAMPLES. (Rus.) Kalinina, I. A. (N. N. Petrov Sci. Res. Inst. Oncol., Leningrad, USSR) and P. P. Dikun. Vop. Onkol. 15(5):95-96, 1969.

The 3,4-benzpyrene (BP) content was determined for 37 salt samples from sea- and lakeside salt mines, 13 samples from salt factories, 3 samples from salt mines and 1 sample of rock salt, from various regions of the USSR. Continuous extraction of 100-200 g salt with distilled benzene or ethyl ether for 10-12 hours was followed by chromatographic fractionation and fluorimetric analysis. BP content varied from 0.008-0.5 $\mu\text{g/kg}$ for the various samples. Before and after drying by direct contact with combustion products of diesel fuel, the BP content from the "Aralsulfat" factory (Kazakh SSR) ranged from 0-0.04 and 0-0.12 $\mu\text{g/kg}$, resp. It is concluded that drying of salts by the direct contact method does not always result in contamination of food with carcinogens.

70-2211 DATA FOR STUDYING THE CARCINOGENICITY OF PRODUCTS FROM PETROLEUM REFINING.

(Rus.) Bruevich, T. S. (Inst. Indust. Hyg. Occup. Dis., Moscow), A. Ia. Khesina and I. A. Ogloblina. Gig. Tr. Prof. Zabol. 13(3):53-54, 1969.

Fluorimetric determinations of the 3,4-benzpyrene (BP) content of petroleum fractions from various parts of the USSR showed that products resulting from high-temperature processes, such as pyrolysis of cracking gas, contained the highest conc. of this carcinogen. The BP content (in $\mu\text{g/kg}$) of fractions from Baku petroleum were: crude tar residue and its acid fraction, 10; Rubrax (asphalt fraction), 26,000; kerosene produced by cracking, 470; cracking bottoms, 4400; cracking residue, 66,000; and hydraulic pyrolysis resin, 39,000,000. The BP content (in $\mu\text{g/kg}$) of fractions from Grozny petroleum were: paraffin distillate, 450; mazut, 6000; gasoline from cracking and flashing condensate, 10; cracking bottoms, 2500; light pyrolysis resin, 2,800,000; and heavy pyrolysis resin, 58,000. The BP content (in $\mu\text{g/kg}$) of fractions from Drogobych petroleum were: medium mineral oil, 900; paraffin filtrate, 1200; paraffin mixture for sweat chamber, 1800; cracking residue, 100,000; coke distillate, 400,000; and kerosene produced by cracking, 0. The BP content (in $\mu\text{g/kg}$) of fractions from high-sulfur Bashkiria petroleum were: gasoline from cracking, 10 and heavy residue from the cracking of mazut, 8600.

70-2212 THE BENZ(α)PYRENE CONTENT IN SOILS AND PLANTS FROM AN AIRPORT. (Rus.)

Smirnov, G. A. (Inst. Exp. Clin. Oncol., Moscow). Vop. Onkol. 16(5):83-86, 1970.

Fluorimetric analysis of extracts from 33 soil samples taken near the runways of the Vnukovo Airport near Moscow showed that the soil contained 1.3-68.0 $\mu\text{g/kg}$ of 3,4-benzpyrene (BP). The BP content was highest in samples taken nearest the runways and was 2-3-fold greater in the upper layer (5-7 cm deep) than in the lower

layer (10-12 cm deep). The BP content of 12 plant samples (mostly timothy grass) ranged from 5.4-21.3 $\mu\text{g/kg}$ and that of 12 root samples ranged from 3.1-7.0 $\mu\text{g/kg}$. The BP content of both soil and plant samples from the airport was significantly higher than for control samples taken from points between Moscow and the airport.

70-2213 CARCINOGENICITY OF SOIL EXTRACTS.

(Rus.) Shcherbak, N. P. (Inst. Exp. Clin. Oncol., Moscow). Vop. Onkol. 16(3):74-78, 1970.

A total of 270 3-mo.-old mice, hybrids of the C57BL and CBA strains which are highly susceptible to carcinogens, were painted on the skin (2-3 admin./week) with 3-4 drops of (1) a concentrated benzene extract of soil taken near a petroleum refinery with a 3,4-benzpyrene (BP) content of 0.22%; (2) a 0.22% soln. of pure BP in benzene; (3) a concentrated benzene extract of soil taken from an old residential area of Moscow (BP content 0.0004%); (4) a 0.0004% BP soln. in benzene; and (5) pure benzene. Only mice in the first 2 groups developed tumors. In group (1), 8 mice had papillomas, 46 had skin cancer, 1 had a sarcoma and 2 had plasmocytomas. In group (2) all 60 animals had skin cancer. Lung metastases were present at autopsy in 5 mice in group (1) and in 10 mice in group (2); in some cases these tumors were multiple. Lymph node metastases were found in 6 mice in group (1) and in 10 mice in group (2). Tumors developed more slowly in group (1) than in group (2).

70-2214 3,4-BENZPYRENE IN DUST SEDIMENT OF ZURICH. (Ger.) Schaad, R. (ETH Inst. Hyg. Indust. Physiol., Zurich, Switzerland) and A. Gilgen. Z. Praev.-Med. 15(2):87-96, 1970.

Between June, 1965 and May, 1966 the av. annual 3,4-benzpyrene (BP) content in the dust sediment of Zurich was 16.8 $\mu\text{g/g}$ dust, compared to a value of 7.5 $\mu\text{g/g}$ dust in a rural area (Klotener Ried). The BP content varied in different zones of the city, and values for industrial zones did not differ significantly from those of other city zones. BP content was higher in winter (20.6 $\mu\text{g/g}$ in the city and 9.0 $\mu\text{g/g}$ in the rural area) than in summer (13.0 $\mu\text{g/g}$ and 6.1 $\mu\text{g/g}$, resp.). Calculation of BP content per area revealed that it was almost 4-fold greater in the city than in the rural area (50.6 $\mu\text{g/m}^2/\text{mo.}$ and 14.3 $\mu\text{g/m}^2/\text{mo.}$, resp.). It is concluded that in comparison to other cities of Europe and the U.S., Zurich is a "clean city" in regard to total amount of dust sediment, but not in regard to BP content of the dust. It was calculated that a person in Zurich inhales as much BP as a cigarette smoker who smokes 5-6 cigarettes/day.

70-2215 3,4-BENZPYRENE CONTENT OF PRUNES DRIED BY DIFFERENT METHODS. (Rus.)

chkovskii, B. S. (Kiev Sci. Res. Inst. Exp. in. Oncol., USSR), Iu. P. Borisiuk, L. A. kti, V. G. Popovskii, M. S. Mordkovich and A. Silich. Gig. Sanit. 34(9):134-135, 1969.

From a comparison of the 3,4-benzpyrene (BP) content of prunes dried by 3 different methods, it is concluded that the use of California tunnel driers or hot air driers is preferable, because fruit dried by these methods contained the smallest amounts of the carcinogen. BP content of prunes dried by these methods was essentially the same, ranging from 1.1-1.5 µg/kg. Blanching reduced the BP content to 1 µg/kg and washing with a 0.03% detergent soln. reduced it to 0.2 µg/kg. In contrast, the BP content was 5.5-16 µg/kg in prunes dried in an oven, in which the fruit was exposed to hot air and smoke from wood burned in an open combustion chamber.

70-2216 ACCUMULATION OF 3,4-BENZPYRENE IN COW AND CALF TISSUES AND IN COW'S MILK WHEN THIS CARCINOGEN IS PRESENT IN THEIR FOOD. (Rus.) Gorelova, N. D. (N. N. Petrov Sci. Res. Inst. Oncol., Leningrad, USSR) and A. I. Cherepanova. Vop. Onkol. 16(3):69-73, 1970.

Small quantities of 3,4-benzpyrene (BP) were found in the livers of two black-variegated cows who were fed supplements of 0.8-1.2 g/day of BP for 80 days. No BP was found in their meat or milk. From an analysis of milk obtained from these cows, it is concluded that there is no relationship between the BP content of the cows' milk and the BP content of their milk. Two calves were fed milk from these cows and were slaughtered at age 100 days. No BP was found in the liver, meat or blood of 1 calf, while the other had BP values approaching those of the controls.

70-2217 EXCRETION OF UNCHANGED 3,4-BENZPYRENE BY RABBITS, COWS AND CHICKENS WHEN IT IS PRESENT IN THEIR FEED. (Rus.) Gorelova, N. D. (N. N. Petrov Sci. Res. Inst. Oncol., Leningrad, USSR) and A. I. Cherepanova. Vop. Onkol. 16(4):108-113, 1970.

From determinations of fecal and urinary excretion of unchanged 3,4-benzpyrene (BP) in rabbits (male), hens and cows fed diets containing BP for 80-153 days, it is concluded that most of the BP is metabolized or possibly absorbed in the g.i. tract. In male rabbits (aged 2.5-3 months), fed BP (86 µg/day) for 153 days, fecal excretion of unchanged BP was higher than that of controls and continued to increase during the experiment. BP was found in 7/15 urine samples. Urinary BP excretion did not increase with time during the experiment. No clear relationship was found between dietary BP and fecal BP excretion in 3 groups of 10 chickens each, fed BP levels of 4.4, 5.9 or 434 µg/day, resp. In 2 cows fed identical quantities of BP (10,000

µg/day), fecal BP excretion was 2409 µg/day and 168 µg/day, resp., after 80 days.

70-2218 PROTON MAGNETIC RESONANCE COUPLING CONSTANTS AND π -BOND ORDERS IN THE ACTIVE REGIONS OF CARCINOGENIC AND NON-CARCINOGENIC POLYCYCLIC HYDROCARBONS. (E.) Bartle, K. D. (U. Leeds, England), D. W. Jones and R. S. Matthews. J. Theor. Biol. 27(1):117-126, 1970.

Proton magnetic resonance studies showed no correlation between the carcinogenic activity of polycyclic hydrocarbons such as 3,4-benzpyrene and 7,12-dimethylbenzanthracene and their ortho coupling constants.

70-2219 METABOLISM OF A NUMBER OF POLYCYCLIC HYDROCARBONS IN NORMAL EMBRYONIC FIBROBLAST CULTURES. (Rus.) Belitskii, G. A. (Inst. Exp. Clin. Oncol., Moscow) and A. Ia. Khesina. Vop. Onkol. 16(4):113-117, 1970.

The carcinogens, 3,4-benzpyrene (BP) and 7,12-dimethylbenzanthracene (DMBA); the noncarcinogens, benz(ghi)perylene (BPL), pyrene (P), and perylene (PL); and dibenzo(a,h)anthracene (DBA; 0.1 µg/ml culture medium) were incubated with first passage mouse embryonic fibroblasts. Hydrocarbons incubated with culture medium, but without cells, served as controls. BP and BA were metabolized rapidly so that practically none of these hydrocarbons were present in the medium or cells after 2 days of incubation. DBA and BPL were metabolized in 5-6 days. After 3 days, 60-70% of the DMBA had been metabolized; observations were discontinued after this because of the great cytotoxicity of this hydrocarbon. After 5 days about 20% of the P and PL still remained unchanged. The rates at which these hydrocarbons were metabolized were not correlated with their carcinogenicity, their solubility in cellular lipids, nor their cytotoxicity. These results cannot be accounted for by the sensitivity of these hydrocarbons to physical or chemical factors such as ozone or UV radiation. It is considered that differences in the rates at which these hydrocarbons are metabolized are dependent upon their ability to induce oxidase activity in the cells.

70-2220 NATURE OF THE WATER-SOLUBLE METABOLITES OF 7,12-DIMETHYLBENZ(a)ANTHRACENE FORMED BY LIVER MICROSOMES OF NORMAL AND 3-METHYLCHOLANTHRENE-TREATED RATS. (E.) Jellinck, P. H. (Queen's U., Kingston, Ontario, Canada), G. Smith and R. Fletcher. Cancer Res. 30(6):1715-1721, 1970.

Liver microsomes were obtained from Sprague-Dawley or Holtzman rats (70-120 days old) which had been admin. 3-methylcholanthrene (MC; 10 mg in sesame oil, p.o.) 24 hours before sacrifice. When incubated with ^{14}C -labeled

7,12-dimethylbenzanthracene (DMBA) in the presence of reduced nicotinamide adenine dinucleotide phosphate (NADPH), the yield of water-soluble radioactivity was paralleled by the yield of hydroxylated DMBA metabolites, and the formation of both types of products was equally affected by inhibitors. Evidence indicates that in MC-treated rats DMBA might be conjugated with glutathione while in normal rats it apparently conjugates with a peptide of relatively low molecular wt. Results obtained with inhibitors indicate that 2 different enzyme systems are involved. Sulfhydryl reagents inhibited DMBA metabolism in MC-treated rat liver but not in that from controls while β -diethylaminoethyl diphenyl-n-propyl acetate was a more potent inhibitor of DMBA metabolism in normal rat liver. It is proposed that the type of conjugate formed depends upon whether DMBA is hydroxylated primarily in the side chain (normal rats) or in the nucleus (MC-treated rats).

- 70-2221 PARTIAL PURIFICATION OF SOLUBLE PROTEIN FROM MOUSE SKIN TO WHICH CARCINOGENIC HYDROCARBONS ARE SPECIFICALLY BOUND. (E.) Tasserou, J. G. (U. Leiden, Netherlands), H. Diringer, N. Frohwirth, S. S. Mirvish and C. Heidelberger. *Biochemistry (Wash.)* 9(7): 1636-1644, 1970.

A method is described for the partial purification of the protein fraction (h protein) of mouse skin, to which carcinogenic hydrocarbons are covalently bound in a quantitative relationship to their carcinogenic activities. The h proteins studied were isolated from the skins of female Swiss albino mice, 48 hours after topical application of ^3H -labeled 1,2,5,6-dibenzanthracene or 3-methylcholanthrene. The h proteins showed a molecular wt. of 40,000 and consisted of 2 similar or identical subunits of molecular wt. 20,000. No h protein was isolated from the skin of mice treated with a non-carcinogenic hydrocarbon (1,2,3,4-dibenzanthracene). It is suggested that the correlation between the carcinogenic process and the binding of the carcinogen to the mouse skin h protein, is better with respect to carcinogenesis than the correlation between carcinogenic activity and the covalent binding of the carcinogen to mouse skin DNA.

- 70-2222 EFFECT OF DIFFERENT DOSES OF 7,12-DIMETHYLBENZ(A)ANTHRACENE ON THE DIFFERENTIATION OF MUSCLE CELL CULTURES. (Rus.) Shuklinov, V. A. (Sci. Res. Inst. Exp. Clin. Oncol., Kiev, USSR). *Vop. Onkol.* 16(5):58-61, 1970.

Trypsinized monolayers of muscle cells from 1-2-day-old rats were incubated with 7,12-dimethylbenzanthracene (DMBA) in conc. of 0.03-6.0 $\mu\text{g/ml}$ of nutrient medium. DMBA was dissolved in acetone so that the final conc. of acetone in the medium was 0.3%. Cultures to which pure acetone had

been added served as controls. At a conc. of 0.03 $\mu\text{g/ml}$, DMBA significantly stimulated muscle cell differentiation; at a conc. of 6.0 $\mu\text{g/ml}$, DMBA significantly inhibited differentiation. The extent to which DMBA inhibited cell differentiation depended upon the time at which the carcinogen was added to the cultures. Inhibition of cell differentiation was more pronounced when DMBA was added earlier.

- 70-2223 THE BINDING OF 7,12-DIMETHYLBENZ(A)ANTHRACENE TO REPLICATING AND NON-REPLICATING DNA IN CELL CULTURE. (E.) Yuspa, S. H. (NCI, Bethesda, Md.), S. del ande Eaton, D. L. Morgan and R. R. Bates. *Chem. Biol. Interactions* 1(2):223-233, 1969/70.

Investigation of the binding of 7,12-dimethylbenzanthracene (DMBA) to DNA from cultured fetal mouse skin cells demonstrated that replication of DNA is not required for binding of DMBA to DNA. Newly synthesized DNA was separated from non-replicating DNA by incubation of the cells with bromodeoxyuridine (BUDR) and ^3H -labeled deoxyadenosine for 15 hours, followed by DNA extraction and CsCl density gradient ultracentrifugation. DMBA binding was found in both newly synthesized heavy DNA and in lighter non-replicating DNA, but there was less binding to newly synthesized DNA. This suggests that a phase of the cell cycle other than the S phase is a more susceptible period for DMBA binding. Although the presence of BUDR in the medium and in the cytoplasm of both replicating and non-replicating cells inhibits DMBA binding appreciably, the presence of BUDR in the DNA molecule did not inhibit hydrocarbon binding. It was also demonstrated that DMBA binding is not an artefact of extraction or that a tritium exchange mechanism was responsible for the observed results.

- 70-2224 ORGAN CULTIVATION OF EMBRYONIC KIDNEY FROM MICE SUBJECTED TO THE TRANSPLACENTAL ACTION OF 7,12-DIMETHYLBENZ(A)ANTHRACENE (DMBA). (Rus.) Sorokina, Iu. D. (Inst. Exp. Clin. Oncol., Moscow). *Biull. Eksp. Biol. Med.* 69(1): 76-80, 1970.

During the last week of gestation 7,12-dimethylbenzanthracene (DMBA) was admin. p.o., either as a single 2-mg dose or at 2 mg/day (total doses of 6 or 10 mg), to female C57BL mice which had been crossed with CBA males. Embryonic kidney explants from mice whose mothers had been given DMBA were more viable than kidney explants from controls and exhibited changes resulting from pronounced epithelial hyperplasia. The increased viability of embryonic kidney cultures was particularly evident when the mothers had been given larger doses of DMBA. Histological changes which developed as a result of the transplacental action of DMBA included multiple cysts on the glomeruli, cystic dilation of the canaliculi with

thickening of the epithelium, hyperchromic merull and tubular structures which resembled remnants of canaliculi. In cultures from oryos whose mothers had received larger doses of DMBA these tubular structures consisted of two types: (1) those which had identical diameters and were located rather close together in the connective tissue stroma and (2) those which were located very close to each other, were hyperchromic and often consisted of cylindrical epithelium in which mitosis was occasionally evident. Detritus was very rarely seen between type (1) tubular structures but was commonly present between type (2) structures.

2225 ULTRASTRUCTURE AND DEVELOPMENT OF EPITHELIAL CELL PSEUDOPODIA IN CHEMICALLY INDUCED PREMALIGNANT LESIONS OF THE HAMSTER POUCH. (E.) Woods, D. A. (Imperial Cancer Res. Fund, London) and C. J. Smith. Exp. Molec. Pathol. 12(2):160-174, 1970.

Syrian golden hamsters (total 20; 4-6 weeks old) were admin. 7,12-dimethylbenzanthracene (DMBA; 5% soln. in liquid paraffin; 3 admin./week x 25 weeks) by topical application to the cheek pouches. Histological examination showed epithelial hyperplasia of the nodules and squamous cell carcinoma induced by DMBA for both the 13- and 25-week groups. One animal showed metastasis to the submandibular lymph node. Epithelial pseudopodia seen in the premalignant state could not be observed when carcinoma developed; theories of this association of pseudopodia and neoplasia are discussed.

2226 INDUCTION OF MAMMARY TUMORS IN RATS WITH AROMATIC HYDROCARBONS. (Rus.) Skrovnyi, A. M. (Inst. Exp. Clin. Oncol., Moscow), A. S. Breslavskii and O. A. Sukacheva. Sov. Onkol. 16(2):59-63, 1970.

Mammary tumors were induced in 200 female Wistar rats (aged 55-65 days) by p.o. admin. of 3 doses each 10 mg in peach oil) of 7,12-dimethylbenzanthracene at 10-12-day intervals. Of these tumors, 14 stopped growing spontaneously, 18 increased in size and 29 underwent complete regression. In 45 of these 61 cases, however, regression was only temporary; the same mammary tumor (12 cases) or another tumor (33 cases) then grew rapidly. Histological examinations of 150 of these tumors showed a progression from fibroadenomatosis to adenomas, adenofibromas and fibroadenomas; to these same tumors with signs of malignant transformation; and finally to cancer. The incidence of cancer increased as the size of the tumor increased.

2227 SUPPRESSION BY SPIRONOLACTONE OF 7,12-DIMETHYLBENZ(a)ANTHRACENE-INDUCED MAMMARY TUMORS. (E.) Kovacs, K. (U. Montreal St. Med. Exp. Surg., Canada) and A. Somogyi. Can. J. Cancer 6(3):195-201, 1970.

Female Sprague-Dawley rats, about 50 days old, were admin. 7,12-dimethylbenzanthracene (DMBA; 40 mg in 2 ml corn oil; single dose p.o.) and some were also admin. spironolactone (SP; 10 mg/100 g body wt.; 2 admin./day x 7 days, beginning 4 days before DMBA admin.; p.o.). Other rats were admin. DMBA (2 mg/day x 3 days, i.v.) and SP (as above). Rats were observed for development of mammary tumors and adrenal changes. After 150 days, 21/24 surviving rats had mammary tumors when admin. DMBA alone, whereas 3/14 animals admin. DMBA + SP developed tumors. There was no marked difference in histological structure of the tumors induced by either treatment; tumors included adenocarcinomas, adenomas and fibroadenomas and they were frequently multiple. The adrenal glands of DMBA-treated rats showed accumulation of calcified scar tissue and necrosis; such changes were not seen in SP-treated rats because it protects the adrenal glands from the adrenocorticolytic effects of DMBA. Rats of the group treated with only 2 mg DMBA/dose showed no significant adrenal changes. It is concluded that SP delays development and decreases frequency of DMBA-induced mammary tumors in rats.

70-2228 BIOCHEMICAL STUDIES IN ADVANCING AND REGRESSING RAT MAMMARY CARCINOMAS INDUCED BY 7,12-DIMETHYLBENZ(a)ANTHRACENE (HUGGINS TUMORS). (E.) Heise, E. (Inst. Cancer Res. Robert Ross Clin., Berlin-Buch), M. Görlich and G. Bacigalupo. J. Nat. Cancer Inst. 45(1):1-10, 1970.

Activities of aspartate transcarbamylase (ATC) and phosphoglucomutase (PGM) and RNA, DNA and protein contents were determined in mammary carcinomas produced by intragastric inj. of female Sprague-Dawley rats, 50-55 days old, with 7,12-dimethylbenzanthracene (DMBA; single 20 mg dose in sesame oil). In most cases oophorectomy or admin. of testosterone propionate (25 mg/kg body wt. in an oily soln.; 3 admin./week, i.m.) caused tumor regression. Mean ATC activities were 2-fold higher in advancing carcinomas than in regressing ones, so that tumor ATC activities may be a suitable parameter for describing the tendency of mammary carcinomas to grow. Tumor PGM activities varied widely in untreated carcinomas and might be indicative of 2 tumor types, but most of these tumors had the rather uniform histologic appearance of cystic papillary carcinomas. PGM activities were uniformly low in testosterone-treated rats, so that this enzyme parameter appears unsuitable for predicting the growth tendency of mammary carcinomas. Regardless of treatment, advancing carcinomas had high RNA/DNA ratios, while regressing carcinomas had low RNA/DNA ratios. No significant differences were found in the protein content of the groups studied. By repeated biochemical analysis of tissue specimens taken serially from the same carcinoma, it was possible to follow directly some of the metabolic changes linked with hormone-induced changes in the growth rates of these mammary tumors.

70-2229 STAINING DIFFERENCES BETWEEN NORMAL AND CARCINOGEN-INDUCED CARCINOMAS IN THE HAMSTER POUCH. (E.) Chavez, R. F. (Loyola U. Dent. Sch., Maywood., Ill.) and P. D. Toto. J. Dent. Res. 49(4):721-724, 1970.

Syrian golden hamsters were admin. 7,12-dimethylbenzantracene (DMBA; 3 admin./week in the right cheek pouch) until tumor development was observed in 10-15 weeks. Squamous cell carcinomas (induced in 89% of the DMBA-treated animals) and normal hamster pouch tissue were observed for alterations in cell surface antigens by fluorescent antibody staining; qualitative results showed decreased staining intensity in the squamous cell carcinomas in comparison to normal epithelial tissue.

70-2230 EFFECT OF TOPICAL CYCLOPHOSPHAMIDE, METHOTREXATE AND VINBLASTINE ON 9,10-DIMETHYL-1,2-BENZANTHRACENE (DMBA) - CARCINOGENESIS IN THE HAMSTER CHEEK POUCH. (E.) Levij, I. S. (Rothschild Hadassah U. Hosp., Jerusalem), J. W. Rwmushana and A. Polliack. Europ. J. Cancer 6(3):187-193, 1970.

Male Syrian golden hamsters (1.5-2.0 mo. old) were admin. various dosages of 7,12-dimethylbenzantracene (DMBA; 1 mg, by topical application) in alternation with liquid paraffin (P), cyclophosphamide (CP; 2.4 mg), methotrexate (MTX; 0.1 mg) or vinblastine (VB; 0.045 mg) over a period of 6 or 12 weeks. Other groups of animals were first admin. DMBA followed 6 or 12 weeks later by the cytostatic drugs for a 6-week period. Hamsters were then examined for development of cheek pouch tumors and other changes. In the group treated simultaneously with carcinogen and cytostatic drugs, invasive squamous cell carcinoma, benign squamous cell papilloma and epithelial hyperplasia were seen in cheek pouches. Intraepithelial carcinoma was seen in 3/7 and 3/7 animals treated with DMBA in alternation with P and CP, resp., after 6 weeks. After 12 weeks, all animals treated with DMBA alone had carcinoma, whereas only some developed carcinoma when treated with P, CP or MTX. Treatment with P or cytostatic drugs, alone, produced no major changes.

70-2231 EFFECT OF DIENESTROL ON THE DEVELOPMENT OF EXPERIMENTAL OSTEOSARCOMA. (Rus.) Kornitskii, M. A. (Orenburg Med. Inst., USSR) and L. A. Cherkasskii. Vop. Onkol. 16(3):84-89, 1970.

Experiments performed on 70 female rabbits showed that s.c. inj. of a 2% dienestrol (D) soln. (0.2-0.3 ml in oil; 2 admin./week) reduced the incidence of osteosarcomas induced by implanting a 10-mg pellet of 7,12-dimethylbenzantracene (DMBA) in the proximal metaphysis of the tibia. D also inhibited the growth of osteosarcomas that did develop in treated animals. Of the 70 rabbits, 20 controls received only DMBA. The 50 experimental animals were divided into 2 subgroups:

40 underwent hysterectomy and salpingectomy (hstx.) and 10 underwent oophorectomy (oov.) before DMBA implantation. D was inj. simultaneously with DMBA or 2 weeks later in the hstx. animals, and 40 days after DMBA implantation in the oov group. Osteosarcomas developed in 10/15 controls, in 8/30 hstx. animals and in 2/8 oov. animals, which survived more than 90 days after DMBA implantation. Fibrous changes were significantly more frequent among D-treated animals than presarcomatous changes and osteosarcomas. Dystrophic changes and necrosis were observed in the osteosarcomas developing in D-treated animals, but were not present in controls. The latent period for osteosarcomas was 95-193 days among controls, 220-910 days among hstx. animals, and 318-353 days among oov. animals.

70-2232 ACTIVITY OF SOME ENZYMES IN THE POISONING OF ANIMALS BY CARCINOGENIC AMINOBIPHENYL DERIVATIVES. (Rus.) Soloimskaja, E. A. (N. N. Petrov Sci. Res. Inst. Oncol., Leningrad, USSR). Vop. Onkol. 16(4):94-98, 1970.

Activities of blood catalase and peroxidase and of liver monoamine oxidase, histaminase and cytochrome oxidase were measured in rats after s.c. inj. of 100 mg/kg body wt. of benzidine, o-tolidine (Tol), 3,3'-dichlorobenzidine (DCB), 3,3'-dihydroxybenzidine (DHB), N,N'-diacetylbenzidine or biphenyl. Enzyme activities were measured (either after a single inj. or 1 admin./week x 2 mo.). After a single inj., benzidine inhibited the activity of all enzymes which catalyze oxidative deamination of endogenous amines while Tol and DCB increased their activity. The activities of enzymes which metabolize serotonin and norepinephrine and activate monoamine oxidase and histaminase were decreased by DHB. Biphenyl and N,N'-diacetylbenzidine had little effect on these enzymes, suggesting that carcinogens which inhibit monoamine oxidase activity act by blocking the pyridoxal phosphate group. All biphenyl derivatives, admin. over a long period, decreased the activity of enzymes which catalyze oxidative deamination of endogenous amines.

70-2233 EFFECT OF INHALATION METHODS FOR ADMINISTERING SOME DISPERSIBLE CARCINOGENS. (Rus.) Zabezhinskii, M. A. (N. N. Petrov Sci. Res. Inst. Oncol., Leningrad, USSR). Biull. Eksp. Biol. Med. 69(1):72-74, 1970.

Exposure of male and female noninbred albino rats to an aerosol of benzidine (BZ; total dose 27 mq; 10-20 mg/m³ x 4 hours; 5 admin./week x 20 weeks) resulted in the development of neoplasms in 8/28 exposed animals; 2 controls developed mammary adenomas after 22 and 26 mo. BZ-exposed animals developed myeloid leukemia (5 cases), mammary fibroadenoma (2 cases) and mammary adenocarcinoma (1 case). The latent period was

18-28 mo. The site and structure of the tumors are essentially the same as those obtained in earlier experiments in which rats were given intratracheal instillations of BZ. BZ did not induce bladder cancer in rats when admin. intratracheally or by inhalation, because the metabolism of aromatic amines in rats is different from the metabolism in man or dogs.

2234 PRECIPITATING FACTORS IN SERUM FROM MICE AFTER FOUR DOSES OF o-AMINOAZOTOLUENE (OAAT). (Rus.) Korosteleva, T. A. L. N. Petrov Sci. Res. Inst. Oncol., Leningrad, (USSR) and L. S. Potapenkova. Vop. Onkol. 15(7): 10-67, 1969.

In the Ouchterlony precipitation test concentrated liver extracts (protein content of 7-8%) from OAAT mice fed 4 doses of o-aminoazotoluene (OAAT) with their food reacted differently with sera from these animals than did normal liver extracts with normal mouse serum. Additional precipitation lines were obtained which were much weaker than the normal precipitation lines and were located closer to the well containing the serum. More intense reactions were obtained, by using a concentrated mouse liver extract which had been reacted in vitro with OAAT to obtain an azo-protein complex, as the antigen. More intense reactions obtained with antigen and serum from treated mice were apparently due to the presence of serum precipitins, or precipitins like them, in the mouse liver antigen. In most experiments no precipitation lines formed when native mouse liver extract, containing 2-3% protein, was used as the antigen. Immunoelectrophoretic reactions of native mouse liver antigens and sera from mice given 4 doses of OAAT were less intense than those occurring between antigen and sera from untreated mice. The content of albumins and γ -globulins was lower and the content of β - and γ -globulins was higher than with normal mouse liver antigen. This suggests that the livers of OAAT-treated mice are deficient in antigenic components present in the normal liver. More intense reactions were obtained when antigen from both normal and treated mice was first reacted in vitro with OAAT. Liver antigen and serum from mice given OAAT for 60 days gave wider and more intense bands in both the albumin and precipitin regions than did antigen and serum from untreated mice.

2235 m-TOLUYLENEDIAMINE CARCINOGENESIS IN RAT LIVER. (Jap.) Hiasa, Y. (Nara Univ., Japan). J. Nara Med. Ass. 21(1):1-19, 1970.

Star rats were admin. m-toluylenediamine (TD; 1% or 0.06% x 30-36 weeks in the diet). Of 3 animals fed 0.1% TD that developed liver carcinoma, 6/9 had metastases to the lymph nodes, testis, lung and epididymis. Concomitant admin. of D,L-ethionine (E) enhanced the formation of

liver tumors, whereas admin. of TD with 3-methylcholanthrene (MC) prevented the development of carcinoma. After i.p. inj. of ^{14}C -TD, radioactivity was highest in the liver, followed by urine, kidney and spleen. Incorporation of ^{14}C -TD was greater in RNA and DNA of non-pretreated liver than in those rats pretreated with p-hydroxypropiophenone, α -naphthyl isothiocyanate, MC or E.

70-2236 A STUDY OF THE EFFECT OF URINARY DIVERSION UPON EXPERIMENTALLY PRODUCED BLADDER TUMORS. (Jap.) Shirai, K. (Kanazawa U. Sch. Med., Japan). Nippon Hinyokika Gakkai Zasshi (Jap. J. Urol.) 61(1):1-27, 1970.

Bladder tumors were induced in 24/50 mongrel dogs, 11-42 mo. after admin. of β -naphthylamine (p.o.). Urinary diversion (UD) was performed and the animals died from 3 to over 6 mo. later. All but 1 UD-treated animal showed malignancy; significant changes were seen in 6/22, and there was no evidence of regression. It is concluded that UD does not inhibit the growth of bladder tumors induced in dogs, although it does reduce urinary symptoms.

70-2237 STUDIES OF THE CARCINOGENIC PROPERTIES OF 3,4-10,11-12,13-TRIBENZFLUORANTHENE IN MICE. (Ger.) Mohr, U. (U. Mainz Inst. Hyg., Germany). Arch. Hyg. Bakt. 153(6):495-510, 1969.

In female NMRI mice, 3,4-10,11-12,13-tribenzfluoranthene (1-50 mg/dose) showed no significant carcinogenic activity, whether admin. by s.c. implant or percutaneously in dimethylformamide, dichloromethane, dioxan or tetrahydrofuran, with or without croton oil as a cocarcinogen. The frequency of skin tumors or tumors of other sites did not exceed the spontaneous tumor rates for these animals. No significant effect was observed with respect to survival time. Although all controls admin. 3,4-benzpyrene percutaneously developed skin tumors, no carcinogenic activity was observed in another group of controls which were treated with 11,12-benzfluoranthene by the same route.

70-2238 NUCLEOPHILIC SUBSTITUTION ON CARCINOGENIC N-ACETOXY-N-ARYLACETAMIDES. (E.) Scribner, J. D. (U. Wisconsin Med. Ctr. McArdle Lab. Cancer Res., Madison), J. A. Miller and E. C. Miller. Cancer Res. 30(6):1570-1579, 1970.

Kinetic studies on the decomposition of ^{14}C -labeled N-acetoxy-N-arylacetamides revealed that the acetoxy group undergoes nucleophilic displacement in aqueous media. In the presence of nucleophiles less basic than the acetate ion, the 2-fluorenyl and 4-stilbenyl N-acetoxyacetamides underwent unimolecular ionization, while the corresponding 4-biphenyl and 2-phenanthryl derivatives appeared to form acetate ion by

bimolecular displacement. In the presence of the more basic trivalent citrate anion, all 4 compounds decomposed at faster rates which approached a max. with increasing nucleophile conc. No correlation was found between the rates of decomposition and the carcinogenic activities of these compounds or of their parent-N-hydroxy derivatives. This is not surprising because of the critical importance in carcinogenesis played by such factors as the rate at which the compound is lost from the inj. site, the rate of penetration of the compound into the target cells, and the rates of degradation and activation of the compound within the target cells.

70-2239 MUTATIONS AND LOSS OF TRANSFORMING ACTIVITY OF *Bacillus subtilis* DNA AFTER REACTION WITH ESTERS OF CARCINOGENIC N-HYDROXY AROMATIC AMIDES. (E.) Maher, V. M., J. A. Miller (U. Wisconsin Med. Ctr. McArdle Lab. Cancer Res., Madison), E. C. Miller and W. C. Summers. Cancer Res. 30(5):1473-1480, 1970.

Reaction of transforming DNA, isolated from cultures of the strain SB19 *Bacillus subtilis*, with the sulfuric acid ester of N-hydroxy-4-acetylaminobiphenyl (OH-AABP) and with the acetic acid esters of N-hydroxy-4-acetylaminostilbene and N-hydroxy-2-acetylaminophenanthrene inactivated transformation and induced mutations of the DNA. These effects were most apparent when DNA was incubated with these esters at 37-53° C, rather than at room temperature. In all cases there was an almost linear relationship between the extent of inactivation (expressed as lethal hits) and the frequency of mutations. In comparison to results obtained previously for the esters of N-hydroxy-2-acetylaminofluorene (OH-AAF), the magnitude of the inactivating and mutagenic activity of the esters depended both upon the nature of the esterified acid and of the aryl group. Sulfuric acid esters of OH-AAF and OH-AABP were more active than the corresponding acetic acid esters. Generally, the relative activities of the esters are inversely related to the stabilities of these esters in aqueous soln. The differences in mutagenic and carcinogenic activity s.c. in rat tissue may be accounted for by differences in the rates of absorption of the compounds into the fibroblasts, their rates of conversion to other forms *in vivo* and the rates of reaction of the acetic acid esters or other derivatives with tissue nucleophiles.

70-2240 EFFECTS OF VARIOUS *IN VITRO* CONDITIONS ON HEPATIC MICROSOMAL N- AND C-OXYGENATION OF AROMATIC AMINES. (E.) Arrhenius, E. (U. Stockholm Wenner-Gren Inst. Exp. Biol.). Chem. Biol. Interactions 1(4):361-380, 1969/70.

An investigation was made of the effects of *in vitro* conditions on the N- and C-oxygenation of the noncarcinogen, dimethylaniline (DMA), by

liver microsomes from male Sprague-Dawley rats in order to clarify the nature and origin of the reactive metabolites of carcinogenic aromatic amines. DMA was used to avoid damage to microsomal detoxication mechanisms which has been observed *in vitro* with low carcinogen conc. The results indicate that in microsomal C-oxygenation, which yields only harmless metabolites, P450 is activated to form a ternary complex with oxygen and substrate by a flavoprotein-catalyzed electron transfer from the amine substrate. The C-oxygenated product is released from P450 without the formation of an intermediary N-oxygenated metabolite by a flavoprotein-mediated electron transfer from reduced nicotinamide adenine dinucleotide phosphate (NADPH). When transfer of electrons from flavoprotein to P450 is inhibited, oxygen enters as a relatively less efficient electron acceptor at the flavoprotein level. During this reaction electrophilic metabolites may be formed which react with nucleophilic centers in adjacent structures. The close correlation of increased N-oxygenation/C-oxygenation ratio *in vitro* with conditions favoring tumor induction *in vivo* and the formation of electrophilic metabolites from the carcinogen, 2-aminofluorene, *in vitro*, indicates that the proposed mechanisms for oxygenation of aromatic amines are relevant for the production of reactive intermediates initiating the tumor-inducing process in chemical carcinogenesis.

70-2241 EFFECTS *IN VITRO* OF 2-AMINOFLUORENE OR ELECTROPHILIC AGENTS ON HEPATIC MICROSOMAL N- AND C-OXYGENATION OF AROMATIC AMINES. (E.) Arrhenius, E. (U. Stockholm Wenner-Gren Inst. Exp. Biol.). Chem. Biol. Interactions 1(4):381-393, 1969/70.

A comparison of the action of the carcinogen, 2-aminofluorene (AF), with that of noncarcinogenic dimethylaniline (DMA) revealed that AF is up to 500-fold more effective than DMA in inhibiting C-oxygenation of DMA by liver microsomes from male Sprague-Dawley rats. In liver microsomes from guinea pigs, which are resistant to the carcinogenic action of aromatic amines, C- and N-oxygenation were equally inhibited. N-acetoxy-2-acetylaminofluorene had almost the same effects as AF on oxygenation in rat and guinea pig microsomes. Preferential inhibition of C-oxygenation produced by methylmercurihydroxide *in vitro* was synergized by pretreatment of rats with 225 mg/kg body wt. i.p. of Celite which mimics adrenal stress induced by carcinogenic amines *in vivo*.

70-2242 INTERACTION OF AROMATIC AMINES WITH RAT-LIVER PROTEINS *IN VIVO*. III. ON THE MECHANISM OF BINDING OF THE CARCINOGENS, N-2-FLUORENYLACETAMIDE AND N-HYDROXY-2-FLUORENYL-ACETAMIDE, TO THE SOLUBLE PROTEINS. (E.) Barry, E. J. (VA Hosp. Lab. Cancer Res., Minneapolis, Minn.), D. Malejka-Giganti and

H. R. Gutmann. Chem. Biol. Interactions 1(2): 139-155, 1969/70.

Stepwise elution from diethylaminoethyl-cellulose was used to separate soluble liver proteins of adult male rats inj. i.p. with equimolar amounts of ^{14}C -N-2-fluorenylacetamide (FAA) or its N-hydroxy derivative (OH-FAA). OH-FAA was bound to all protein fractions by a 2-2.5-fold greater extent than FAA. The radioactivity of both compounds was bound preferentially to a group of weakly basic proteins eluted in fraction 2. Preferential binding was partially accounted for by interaction of methionine with a positively charged amidonium ion from OH-FAA, indicating that 50% of the FAA adducts are formed via N-hydroxy-FAA. Protein hydrolysates also yielded ^{14}C -labeled 2-fluorenamine (FA), FA-9-one and 3-methylthio-2-fluorenamine. These compounds accounted for 4% of the total protein-bound radioactivity, or for 13-20% of the adducts which did not carry the acetyl group of OH-FAA. Most of the bound radioactivity of FAA and of OH-FAA remained unidentified. In vitro reaction of OH-FAA with soluble liver proteins yielded labeled adducts which lacked the acetyl group of the hydroxamic acid. These adducts were formed by interaction of 2-nitrosofluorene (and, by inference, of 2-fluorenylhydroxylamine) with the proteins, and also contributed to in vivo adduct formation.

70-2243 MODIFICATIONS OF RIBONUCLEIC ACID BY CHEMICAL CARCINOGENS. II. IN VIVO REACTION OF N-2-ACETYLAMINOFLUORENE WITH RAT LIVER RIBONUCLEIC ACID. (E.) Agarwal, M. K. (Columbia U. Coll. Physicians Surg., New York, N. Y.) and I. B. Weinstein. Biochemistry (Wash.) 9(3):503-508, 1970.

Examination of the in vivo binding of radioactive N-2-fluorenylacetamide (FAA) and N-hydroxy-2-FAA to rat liver transfer RNA (tRNA) revealed that the tRNA had 2-3-fold the specific activity of 5S, 18S and 28S RNA. FAA and OH-FAA were bound preferentially to rat liver tRNA in contrast with ribosomal RNA (rRNA). Study of the kinetics of FAA binding to both tRNA and rRNA showed max. binding at 24 hours post-inj. A higher specific activity for tRNA than rRNA occurred within the first 24 hours and was followed by a rapid decline of tRNA activity, resulting in comparable activity of both RNA types at 48 hours; these activities declined with half-life values of about 5 days. Separation of FAA-tRNA from unmodified tRNA was performed by chromatography on benzoylated diethylaminoethyl-cellulose columns. Further characterization of FAA-tRNA demonstrated that it reacts with several types of tRNA in vivo. Studies using in vivo orotic acid labeling of RNA to examine the effect of FAA diet on the profile of newly synthesized tRNA resulted in the conclusion that dietary FAA binds to only a very small fraction of the newly synthesized RNA.

70-2244 ON THE MECHANISM OF ACTION OF CARCINOGENIC AROMATIC AMINES. I. BINDING OF 2-ACETYLAMINOFLUORENE AND N-HYDROXY-2-ACETYLFLUORENE TO RAT-LIVER NUCLEIC ACIDS IN VIVO. (E.) Kriek, E. (Netherlands Cancer Inst., Amsterdam). Chem. Biol. Interactions 1(1):3-17, 1969/70.

Male, white strain R-Amsterdam rats (300 g) and, in one experiment, females of the same strain were partially hepatectomized. Some were fed a diet containing N-2-fluorenylacetamide (FAA; 0.04% x 8 mo. before inj. of labeled compounds) which induced a high frequency of tumors after 7-9 mo. Inj. of ^{14}C -labeled N-2-aminofluorene (AF). FAA, N-hydroxy-FAA and N-hydroxy-N-acetyl-AF was performed at the same dose level (10 mg/kg; i.p.) for all compounds. Binding of AF or FAA to ribosomal RNA (rRNA) or DNA resulted in few differences after inj. of FAA, AF or N-hydroxy-FAA; inj. of N-hydroxy-FAA gave 3-fold greater binding values for N-hydroxy-FAA when compared to FAA. Binding of FAA after inj. of N-hydroxy-N-acetyl-AF was similar to that for inj. of N-hydroxy-FAA. Differences existed for male and female rats and their response to FAA, with 3.6-fold less binding of FAA to rRNA in the females. It is concluded that the extent of binding of the acetyl derivatives to rRNA correlates with their carcinogenicity.

70-2245 CODING AND CONFORMATIONAL PROPERTIES OF OLIGONUCLEOTIDES MODIFIED WITH THE CARCINOGEN N-2-ACETYLAMINOFLUORENE. (E.) Grunberger, D. (Inst. Cancer Res., New York, N. Y.), J. H. Nelson, C. R. Cantor and I. B. Weinstein. Proc. Nat. Acad. Sci. USA 66(2): 488-494, 1970.

Mechanisms by which attachment of N-2-fluorenylacetamide (FAA) to guanosine residues in nucleic acids distorts their structure and changes their biological activity were studied. Oligonucleotides were modified with N-acetoxy-FAA, repurified by paper chromatography, and their base composition analyzed spectrophotometrically after treatment with RNase and thin-layer chromatography on cellulose plates. Determination of the abilities of these oligonucleotides to stimulate binding of ^{14}C -valyl-transfer RNA to ribosomes showed that FAA residues bound to guanosine in oligonucleotides of guanosine phosphate, uridine phosphate and uridine (GpUpU); adenosine phosphate, adenosine phosphate and guanosine (ApApG); or a random copolymer of 3 parts uridylic acid to 1 part guanylic acid (poly UG) inactivates their function in codon recognition. Circular dichroism spectra suggest that this is caused by gross conformational changes in these compounds. The relationship of these findings to the carcinogenic activity of FAA is not known.

70-2246 INHIBITORS OF CHEMICAL CARCINOGENS AS PROBES FOR MOLECULAR TARGETS: DNA AS DECISIVE RECEPTOR FOR METABOLITE FROM N-HYDROXY-

N-2-FLUORENYLACETAMIDE. (E.) Matsushima, T. (Nat. Cancer Ctr. Res. Inst., Tokyo) and J. H. Weisburger. Chem. Biol. Interactions 1(2): 211-221, 1969/70.

Effects of prefeeding inhibitors of the hepatocarcinogenicity of N-2-fluorenylacetamide (FAA) on carcinogen binding to liver macromolecules were studied, after a single i.v. inj. of the intermediate metabolite, ^{14}C -labeled N-hydroxy-FAA, in male Fischer F344 rats. Carcinogen binding to liver nuclear DNA was reduced significantly by feeding 8-week-old rats chloramphenicol, acetanilide, m-acetotoluidide, or indole for 4 weeks (0.8-2% in diet). Methionine, p-acetotoluidide, tyrosine, inosine and guanine had no significant effect. Carcinogen binding to ribosomal RNA was decreased by indole, m- and p-acetotoluidide, L-tryptophan, guanine and inosine. Feeding of acetanilide and m- and p-acetotoluidide increased binding to soluble RNA. Chloramphenicol depressed, but indole and m- and p-acetotoluidide increased binding to microsomal proteins. Admin. of chloramphenicol, acetanilide, tryptophan and tyrosine slightly decreased binding to soluble proteins while admin. of indole and m- and p-acetotoluidide increased it. These results support the hypothesis that DNA is a key receptor of chemical carcinogens in tumor initiation. However, it is also possible that carcinogens bind to some specific enzymes involved in DNA synthesis, repair and transcription.

70-2247 METABOLIC AND MORPHOLOGIC STUDIES OF HEPATOCARCINOGENESIS IN THE RAT. (E.) Peraino, C. (Argonne Nat. Lab., Argonne, Ill.) and R. J. M. Fry. Argonne Nat. Labs. Ann. Rep. ANL-7535:39-42, 1968.

Follow-up studies of prolonged feeding of N-2-fluorenylacetamide (FAA) to male, weanling Charles River rats showed increased hepatocyte proliferation followed by hepatocellular carcinomas with surrounding hepatocyte proliferation. Examination of enzyme activity in different pieces of rat liver revealed that both ornithine aminotransferase and serine dehydratase showed variable responses suggestive of a regulatory activity that had been altered during carcinogenesis. When phenobarbital was fed in the diet after FAA admin., hepatoma production was enhanced as compared to results for simultaneous feeding.

70-2248 METABOLIC AND MORPHOLOGIC STUDIES OF HEPATOCARCINOGENESIS IN THE RAT. (E.) Peraino, C. (Argonne Nat. Labs., Argonne, Ill.), R. J. M. Fry and E. Staffeldt. Argonne Nat. Labs. Ann. Rep. ANL-7635:131-133, 1969.

Male, 6-week-old SD/Anl [Anl 66] rats were fed N-2-fluorenylacetamide (FAA; 0.02% in the diet x 2, 4, and 6 weeks) and some were fed phenobarbital (Ph; 0.5% in the diet); the development of

hepatomas was observed. Frequency of tumor was greater in rats fed FAA + Ph, although the 6-week group had results similar to those without Ph admin. CRL:CD(SC) rats, 6 weeks old, were fed a diet of FAA (0.01% and 0.02%) and Ph (as above), and autoradiography showed greatest increase of liver cells for 0.01% FAA + Ph admin. It is concluded that Ph amplified the carcinogenic action of FAA when admin. after FAA in the diet.

70-2249 COMPARISON OF THE EFFECT OF THE CARCINOGEN N-HYDROXY-N-2-FLUORENYL-ACETAMIDE IN INFANT AND WEANLING RATS. (E.) Weisburger, J. H. (NCI, Bethesda, Md.), M. Klein, E. K. Weisburger, R. M. Glass, G. Woodard and M. T. I. Cronin. J. Nat. Cancer Inst. 45(1): 29-35, 1970.

Male and female, 3-day-old Fischer rats were admin. N-hydroxy-N-2-fluorenylacetamide (OH-FAA; 27 mg/kg, 3 admin./week x 4 weeks, by gastric intubation) and, after weaning, were admin. OH-FAA in the diet (67.5-216 ppm x more than 12 weeks). Weanling and adult rats were also admin. OH-FAA (12 intragastric admin., then in the diet). Survival of all rats was generally good. All rats admin. OH-FAA in the diet gained less wt. than controls, but showed increases in liver and spleen wt. Rats treated with OH-FAA by stomach tube when from 3-30 days of age, followed by admin. in the diet, all developed liver tumors with some metastases to the lung, carcinoma of the ear duct and urinary bladder, squamous carcinoma of the stomach, sarcoma of the forestomach and urinary bladder papillomas. Rats admin. OH-FAA in 12 doses by stomach tube only during infancy developed no neoplasms.

70-2250 MODIFICATIONS OF RIBONUCLEIC ACID BY CHEMICAL CARCINOGENS. I. IN VITRO MODIFICATION OF TRANSFER RIBONUCLEIC ACID BY N-ACETOXY-2-ACETYLAMINOFLUORENE. (E.) Fink, L. M. (Columbia U. Coll. Physicians Surg., New York, N. Y.), S. Nishimura and I. B. Weinstein. Biochemistry (Wash.) 9(3):496-502, 1970.

Reaction of N-acetoxy-2-fluorenylacetamide (N-acetoxy-FAA; $0.3-30 \times 10^{-3}$ M) with 1.3 mg/ml Escherichia coli B transfer RNA (tRNA) in vitro resulted in substitution of tRNA with FAA residues (FAA-tRNA). The amino acid acceptance capacity of E. coli tRNA after treatment with N-acetoxy-FAA was studied for 14 amino acids; the activity for arginine and lysine tRNA was inhibited to the greatest extent. Chromatographic behavior of FAA-tRNA on diethylaminoethyl (DEAE)-Sephadex and benzoylated DEAE-cellulose columns showed that 33% of E. coli methionine tRNA failed to react with N-acetoxy-FAA and that the remaining 66% formed at least 2 derivatives. It is hypothesized that the functional modifications in nucleic acids produced by N-acetoxy-FAA

result from a change in nucleoside conformation from "anti" to "syn."

0-2251 STRUCTURE-ACTIVITY RELATIONSHIPS OF N-ACYLARYLHYDROXYLAMINES IN THE RAT. (E.)

utmann, H. R. (VA Hosp. Lab. Cancer Res., Minneapolis, Minn.), D. S. Leaf, Y. Yost, R. E. Sydell and C. C. Chen. Cancer Res. 30(5):485-1498, 1970.

The carcinogenicity of aromatic amides and N-acylarylhydroxylamines (AHA) was tested in male and female Holtzman rats (60-100 g). Compounds were inj. i.p. (2.3 or 4.5 mg/100 g body wt.; 3 admin./week x 4 weeks) in a soln. of 0.9% NaCl and acacia or were admin. through a stomach tube (8.0 mg/100 g body wt.; 3 admin./week). The observation period was 12 mo. The toxicity of AHA varied greatly and was not related to their structure or carcinogenicity. The carcinogenicity of arylamides was increased several-fold by synthetic N-hydroxylation, supporting the hypothesis that metabolic N-hydroxylation activates arylamides and may be obligatory for the induction of mammary and other tumors. However, carcinogenicity was limited to AHA in which the aromatic ring was a fluorene or biphenyl system. In contrast to N-hydroxy-2-fluorenylacetamide previously found to be a mammary carcinogen for female, but not for male, rats when inj. i.p.) the 3-fluorenyl isomer was a weaker carcinogen but induced mammary tumors in rats of both sexes. N-hydroxy-1-fluorenylacetamide and N-hydroxy-1-fluorenylbenzamide were also highly active in inducing mammary tumors (often benign) in immature females after a long latent period. N-hydroxy-4-biphenylbenzamide was a potent mammary carcinogen while N-hydroxy-2-fluorenylbenzamide (OH-FBA) produced sarcomas at or near the site of admin., suggesting that relatively subtle changes in molecular structure may affect the site and possibly the mode of action of these carcinogens. Tumor frequency after p.o. admin. of OH-FBA was the same (75%) as that observed after i.p. inj. Most of the tumors (70%) were squamous cell carcinomas of the forestomach derived from the surface epithelium. The parent amide, N-2-fluorenylbenzamide, was noncarcinogenic.

-2252 PHENOTYPIC REVERSION BY HYDROXYLAMINE: A NEW GROUP OF SUPPRESSIBLE PHAGE T4 RII MUTANTS. (E.) Levisohn, R. (Tel Aviv U., Israel). Genetics 64(1):1-9, 1970.

When T4 rII mutants were exposed *in vivo* to hydroxylamine (HA; 10^{-3} M), 8/105 showed phenotypic reversion (the ability to grow on *Escherichia coli* KB) although their progeny were found to retain the rII genotype. Comparison with phenotypic reversion by 5-fluorouracil, which probably acts at the level of messenger RNA (mRNA), supports the conclusion that HA causes phenotypic reversion by affecting rII mRNA. Since none of the previously classified rII

mutants, having either uracil, adenine, cytosine or guanine at the mutated site, showed phenotypic reversion by HA, it is concluded that the ability to be phenotypically reverted by HA requires a certain mutant sequence (i.e., the mutant base has to be next to a given base).

70-2253 ACUTE CHANGES IN NUCLEIC ACID AND PROTEIN SYNTHESIS IN THE MOUSE BLADDER EPITHELIUM INDUCED BY THREE BLADDER CARCINOGENS. (E.)

Lawson, T. A. (U. Queensland Med. Sch., Brisbane, Australia), K. M. Dawson and D. B. Clayson. Cancer Res. 30(6):1586-1592, 1970.

RNA and DNA synthesis was stimulated in the bladders of mice by a single p.o. dose of 4-ethylsulfonylnaphthalene-1-sulfonamide (ENS; 0.5 mg), 2-acetylaminofluorene (AAF; 4 mg), or 3-aminodibenzofuran (ABF; 2 mg). These 3 carcinogens stimulated nucleic acid synthesis, but the magnitude and timing of the response was different in each case. Quantitative comparisons could not be made because different mouse strains and different carcinogen doses were used. It is concluded that increased DNA synthesis is probably a response to chemically-induced cellular injury. When added to the diet, AAF did not produce a lasting increase in DNA synthesis in the bladder. With ENS, the number of mice responding to the stimulus decreased as the feeding continued. Thus, maintenance of a high level of DNA synthesis does not appear necessary in bladder carcinogenesis. A single p.o. dose of ENS had no effect on nucleic acid synthesis in the liver; AAF stimulated both RNA and DNA synthesis in the liver; ABF caused a small increase in hepatic DNA synthesis in males, but not in females.

70-2254 EARLY CHANGES IN THE FINE STRUCTURE OF RAT-BLADDER EPITHELIUM INDUCED BY 4-ETHYLSULFONYLNAPHTHALENE-1-SULPHONAMIDE. (E.)

Hicks, R. M. (Middlesex Hosp. Med. Sch. Bland-Sutton Inst. Path., London). Chem. Biol. Interactions 1(1):49-71, 1969/70.

Changes in the fine structure of the female Wistar rat bladder transitional epithelium, developing 2 hours-5 days after admin. of 1 dose of 4-ethylsulfonylnaphthalene-1-sulfonamide (ESNS; 5 mg), were examined with both the light and electron microscopes. Necrosis, followed by hyperplasia, occurred in focal areas of the bladder epithelium. Initial damage was most pronounced in superficial cells which revealed proliferation of the Golgi complex, increased production of lysosomes and autophagic vacuoles, and subsequent dissolution of large areas of cytoplasm. Mitotic rate increases in basal and intermediate cells compensated for superficial cell loss; epithelium depth increased from 3 to 4 or 5 cell layers. Extracellular spaces dilated and the thickened, rigid, luminal barrier membrane was replaced by a thinner more flexible

one in surviving superficial cells. This new membrane seems to be more permeable than normal and permits water flow through the epithelium. It is suggested that ESNS-treated bladders are more susceptible to chemical carcinogenesis because of their damaged luminal barrier membrane.

70-2255 TRANSFER RNA PATTERNS IN LIVERS OF RATS FED DIETS CONTAINING 3'-METHYL-4-DIMETHYLAMINOAZOBENZENE. (E.) Goldman, M. (U. Texas M. D. Anderson Hosp. Tumor Inst., Houston) and A. C. Griffin. *Cancer Res.* 30(6):1677-1680, 1970.

Female Sprague-Dawley rats (150-175 g) were fed a diet containing 0.06% 3'-methyl-4-dimethyl-aminoazobenzene (MeDAB) for 8 weeks. By this time the livers of these animals were enlarged, fibrotic and cirrhotic, but no evidence of tumors was found on gross examination. Transfer RNA (tRNA) prepared from the livers of MeDAB-treated rats and controls was methylated *in vitro* with diazomethane and the resulting methylated tRNA was charged with ^{14}C - or ^3H -labeled amino acids. Liver aminoacyl tRNA formed in this way was cochromatographed with aminoacyl tRNA from controls and with methylated tRNA on reversed phase columns. Major differences were observed in the lysyl, leucyl, phenylalanyl and tyrosyl patterns of MeDAB-treated animals and controls. These differences may be due to differences between tRNA from altered liver cells and that from normal liver cells. It is also possible that altered tRNA has undergone methylation or has reacted with N-hydroxylated or other metabolites of MeDAB. There was little difference in the arginyl-, seryl-, methionyl-, valyl-, histidyl- and threonyl-tRNA patterns in normal and pre-cancerous rat liver.

70-2256 THE DISTRIBUTION AND SYNTHESIS OF DNA IN TWO CLASSES OF RAT LIVER NUCLEI DURING AZO DYE-INDUCED HEPATOCARCINOGENESIS. (E.) Sneider, T. W. (Baylor Coll. Med. Texas Med. Ctr., Houston), D. E. Bushnell and V. R. Potter. *Cancer Res.* 30(6):1867-1873, 1970.

Changes in the DNA content and in DNA synthesis were studied in hepatocyte nuclei and stromal nuclei from liver homogenates obtained from adult male Sprague-Dawley rats fed a diet containing 0.05% by wt. of 3'-methyl-4-dimethyl-aminoazobenzene for 42 days. Although 80% of the DNA was associated with hepatocyte nuclei at the beginning of the experiment, only about 25%

could be recovered from this fraction after 14 days. At the end of the experiment liver DNA was distributed almost equally between hepatocyte and stromal nuclei. DNA synthesis did not increase until 14 days after dye feeding began, although the ratio of DNA in hepatocyte nuclei to DNA in stromal nuclei did change. Although both hepatocyte and stromal nuclei incorporated a large amount of ^3H -thymidine (^3H -Tdr) into their DNA after 14 days, little of the labeled DNA could be recovered from livers of rats (given inj. of ^3H -Tdr early in the experiment) examined after 42 days on the dye diet. These findings emphasize the extremely complex nature of changes occurring during the early stages of liver cancer induced by azo dyes.

70-2257 AUTORADIOGRAPHIC STUDY OF THYROID CARCINOGENESIS IN RATS TREATED WITH ^{131}I AND METHYLTHIOURACIL. (Bul.) Khristov, K. (Sci. Res. Inst. Oncol., Sofia, Bulgaria). *Onkologiya* 6(2):53-58, 1969.

Measurements of protein-bound ^{131}I (PBI) were made on thyroids from male and female albino rats which were admin.: (1) a single dose of 30 μC of ^{131}I , i.p.; (2) 15 mg/day of methylthiouracil (MTU) p.o. through a tube; or (3) ^{131}I followed, 24 hours later, by MTU. Controls and ^{131}I -treated animals were inj. with 50 μC of ^{131}I 24 hours before sacrifice, 365-450 days after the beginning of the experiment. Rats in groups (2) and (3) were given the final dose of ^{131}I 14 days after discontinuation of MTU. In both controls and treated animals, PBI was distributed unevenly among the thyroid follicles. Rats treated with ^{131}I alone developed morphological changes in the thyroid epithelium which corresponded to those occurring during carcinogenesis. The uneven distribution of PBI in the glandular parenchyma of these animals was probably due to differences in the colloid content of the individual follicles and not to a loss of the ability of epithelial cells to bind ^{131}I . A total of 52 epithelial thyroid tumors developed in group (2) and (3) animals: 2 follicular carcinomas, 5 trabecular tumors, 9 papilliferous tumors, and 36 follicular tumors. Only small amounts of PBI were found in most of these tumors. For the most part, only colloid-producing follicular tumors contained PBI. Follicles containing PBI were usually small and lined with high cuboidal or columnar epithelium. Little PBI was found in follicles lined with low cuboidal epithelium.

258 SELECTIVE REMOVAL OF RIBONUCLEIC ACID RESPONSIBLE FOR HYPERBASOPHILIA AT LIVER PARENCHYMA DURING AZO DYE CARCINOGENESIS. (E.) Brière, N. (U. Sherbrooke, Quebec, Canada). *J. Histochem. Cytochem.* 18(7):503, 1970.

Wistar rats (200 g) were admin. 4-dimethylaminobenzene (0.06% in the diet x 180 days) preneoplastic areas and tumors of the liver were defined histologically. Intense RNA staining of cytoplasmic hyperbasophilia, possibly representative of malignant transformation, were observed; mild RNase treatment showed selective lysis and a masking of cytoplasmic protein in the preneoplastic sites. It is suggested that the hyperbasophilia results from the presence of RNA (either normal-type or an altered type in excess) particularly sensitive to mild RNase treatment.

259 CHARACTERISTIC ULTRASTRUCTURE OF HEPATOMAS INDUCED BY AZO DYES IN WISTAR RAT: PRESENCE OF ANNULATE LAMELLAE IN THE TRANSPLANTABLE N-13 HEPATOMA. (Sp.) G. Bart, A., Jr. (U. Valencia Sch. Med., Spain) and A. Peydro. *Med. Esp.* 62(364):41-61, 1969.

Electron microscopic study of tumor fluid from a hepatoma induced by 4-dimethylaminobenzene (no details) in Wistar rats was studied by electron microscopy after centrifugation and cellular sedimentation procedures. Formation of fenestrated membranes (annulate lamellae) in the cytoplasm of transplanted hepatoma cells was seen; membranes were joined to the rough endoplasmic reticulum. Annulate lamellae were similar in structure to those of embryonic cells of lower animals or cells of experimental tumors.

260 EFFECT OF BASIC CUPRIC ACETATE ON THE BIOCHEMICAL CHANGES IN THE LIVER OF THE RAT FED CARCINOGENIC AMINOAZO DYE. II. ACTIVITY AND ISOZYME PATTERN OF LACTATE DEHYDROGENASE. (E.) Yamane, Y. (U. Chiba, Japan), K. Imai, M. Hayashi, M. Matsuzaki and A. Hanaki. *J. Pharm. Bull. (Tokyo)* 18(5):1050-1052, 1970.

Male Wistar rats (100-150 g) received 4-dimethylaminobenzene (DAB 0.09%) and/or 0.5% cupric acetate hexahydrate in their diet. Liver homogenates were assayed for total lactate dehydrogenase (LDH) and LDH isoenzyme activity. There was a decrease in total LDH activity, probably secondary to the reduction in LDH isoenzyme 5, as well as the previously unobserved appearance of LDH isoenzyme 3. These changes were observed with admin. of DAB alone, but not with DAB + cupric ion.

261 ACTIVITY OF GLUCOSE PHOSPHORYLATING ENZYMES IN RAT LIVER DURING THE EARLY

STAGES OF CARCINOGENESIS. (Uk.) Rubenchik, B. L. (Sci. Res. Inst. Nutr. Hyg., Kiev, USSR) and M. B. Pliss. *Ukr. Biokhim. Zh.* 41(5):493-497, 1969.

The activities of glucose phosphorylating enzymes were determined in the homogenates, mitochondria and hyaloplasm of the livers of male rats fed 4-dimethylaminobenzene (DAB; 0.06% in the diet) hexokinase and glucokinase activities were determined in hyaloplasm after dialysis. Determinations were run after 2, 10, 18 and 24 weeks of DAB feeding. No significant changes occurred in enzyme activity during the early stages of carcinogenesis (up to 18 weeks). However, the total enzyme activity in rat liver homogenate and mitochondria increased almost 3-fold and in the hyaloplasm, 2.3-fold, after 24 weeks when the rats had tumors visible on gross examination of the liver. This increase was caused by increased hexokinase activity; glucokinase activity remained unchanged. No significant changes occurred in the Michaelis constant for hexokinase or in the K_i value for inhibitor (adenosine diphosphate).

70-2262 ANAEROBIC GLYCOLYSIS AND PATTERNS OF GLYCOLYTIC INTERMEDIATES DURING LIVER CARCINOGENESIS AND IN HEPATOMA. (E.) Gaja, G. (U. Milan Inst. Gen. Path., Italy), F. Cajone, M. E. Ferrero and A. Bernelli-Zazzera. *J. Nat. Cancer Inst.* 44(6):1269-1280, 1970.

When tissue slices from transplantable rat hepatomas were preincubated for short periods with oxygen, a significant increase occurred in the rate of anaerobic glycolysis in the presence of 30 mM glucose with Morris hepatoma 5123 but not with Morris hepatomas 3924A, 7288C and 7793. During the entire period of treatment, glycolytic stimulation was detected in liver slices from male Wistar rats fed a diet containing 4-dimethylaminobenzene (DAB). However, the extent of this stimulation was reduced and was not correlated with the duration of treatment. DAB also increased the basal rate of glycolysis and the rate of glycogenolysis. When hepatomas developed after 5-6 mo., the liver glycogen content suddenly dropped. Changes in the conc. of glycolysis intermediates, particularly fructose diphosphate (FDP), triose phosphate (TP), α -glycerolphosphate and 3-phosphoglycerate, suggest that hepatoma glycolysis is not restrained by the "bottleneck" which, in non-preincubated liver slices, limits the anaerobic flow of metabolites after triose phosphate, and which is removed by oxygen preincubation. Since conc. of FDP and TP increase in non-preincubated liver slices from DAB-fed animals, it is assumed that high rates of basal glycolysis in these rats depend upon factors other than those responsible for glycolytic stimulation. Increased glycogenolysis and the high phosphofructokinase activity found in DAB-treated rats might play an important role, but

alternative possibilities cannot be ruled out.

- 70-2263 GLYCOLYSIS RATE AND ACTIVITY OF REGULATING ENZYMES IN RAT LIVER HYALOPLASM WHEN LIVER CARCINOGENS AND THE HERBICIDE, MONURON, ARE ADMINISTERED. (Rus.) Rubenchik, B. L. (Sci. Res. Inst. Nutr. Hyg., Kiev, USSR). Bull Eksp. Biol. Med. 69(3):61-63, 1970.

The glycolysis rate and phosphofructokinase (PFK) and hexokinase (HK) activities were determined in the liver hyaloplasm of adult male albino rats admin. 4-dimethylaminoazobenzene (DAB) or thioacetamide (TA) (dose unspecified) in the diet or Monuron (3-(p-chlorophenyl)-1,1-dimethylurea; 450 mg/kg, route unspecified). After 24 weeks all the DAB- and TA-treated rats had hepatomas, but no tumors were found in Monuron-treated animals after 18 weeks. At first the glycolysis rate tended to decrease, but within 18 weeks it increased greatly in DAB- and TA-treated rats and, to a lesser extent, in Monuron-treated animals. The PFK activity remained unchanged after 2 weeks of DAB and TA admin., but decreased after Monuron. After 10 weeks PFK activity decreased markedly in DAB- and TA-treated rats. Differences between HK activity in experimental animals and controls became evident only in the late stages of cancer development when it increased sharply after DAB and TA admin.

- 70-2264 CANCER AND HORMONAL SECRETION. (Jap.) Minakami, T. (U. Kanazawa Sch. Med., Japan), T. Nishio, J. Kobayashi, H. Shima, K. Fujii, T. Nagaharu and Y. Nakajima. Hormon to Rinsho (Clin. Endocr. (Tokyo)) 16(9):679-684, 1968.

Admin. of 4-dimethylaminoazobenzene (DAB; 0.06% in the diet x 20 weeks) to 10 orchietomized (orx.) male Wistar rats, 9 orx. rats inj. with estrogen (25% diethylstilbestrol-cholesterol; 50 mg) and 10 controls induced liver cancer in 40%, 66.6% and 50%, resp. DAB conc. in the liver was highest after 6 weeks in the orx. rats and after 4 weeks in controls. When 7,12-dimethylbenzanthracene (10 mg s.c.) was admin. to 23 orx. male Wistar rats, 12 orx. and estrogen-treated rats, and 15 controls, all animals developed tumors by 70 days. Sarcomas developed in 4 mo. in 65.2%, 66.6% and 60.0%, resp. The av. pituitary wt./100 g body wt. was 7.5 mg, 9.3 mg and 4.3 mg, resp., for the 3 groups. Av. adrenal wt. was 4.5 mg, 6.6 mg and 11.5 mg, resp. Tumor growth was greatest in orx., estrogen-treated rats.

- 70-2265 THE EFFECT OF HYPOPHYSECTOMY ON THE EXPERIMENTAL PRODUCTION OF RAT THYROID NEOPLASMS. (E.) Nadler, N. J. (McGill U., Montreal, Quebec, Canada), M. Mandavia and M. Goldberg. Cancer Res. 30(6):1909-1911, 1970.

A study of inbred female CDF Fischer rats demonstrated that thyroid follicular cell neoplasms do not develop after i.p. inj. of 3 μ C 131 I and/or a low-iodine diet in the absence of thyroid-stimulating hormone (TSH). Hypophysectomized (hypox.), sham-hypox. and nonoperated rats were inj. with 131 I or not inj. and then given a low-iodine diet with or without an iodine supplement. After 6 mo. follicular cell neoplasms were found in 96% of the sham-hypox. rats given 131 I and a low-iodine diet. The mean number of neoplasms was 5.5/animal and the mean aggregate neoplasm vol. was $0.57 \times 10^8 \mu^3$ /thyroid gland. No thyroid follicular cell tumors developed in sham-hypox. rats given 131 I alone or in hypox. rats given a low-iodine diet alone, 131 I alone, or a combination of both. It is concluded that the anterior pituitary gland, presumable through secretion of TSH, is a prerequisite for the development of thyroid follicular cell neoplasms; it is probably essential to maintain the tumors and make them grow, but it would appear unnecessary once the neoplasms become autonomous.

- 70-2266 THE EFFECT OF ENVIRONMENT ON THE GROWTH AND FUNCTION OF RAT THYROID TRANSPLANT TUMOURS. Matovinovic, J., M. S. Leahy, W. F. Armstrong and H. C. Hill. Pp. 211-248 in Thyroid Neoplasia, Young, S. and D. R. Inman (Eds.). Academic Press, London, 1968, 470 pp.

Highly inbred 6-week-old Fischer rats, fed an iodine-deficient diet for 2 wk. and thyroidectomized by 131 I, were implanted s.c. with nodular goiter tissues from male rats which had received iodine-deficient diets for 16-24 months. The rats developed palpable tumors in the transplanted nodules after 3 weeks-6 months; after the second transplant generation, the tumors grew in both thyroidectomized-iodine-deficient rats and intact rats on a normal diet. Thyrotropin (T), a biological environmental factor, was both a tumor-inducing and promoting agent, indicating a response of genetic factors to varying levels of T. It is assumed that in susceptible persons (those with prolonged or severe iodine deficiency and increased requirements for thyroid hormone, combined with disturbance of hormone synthesis, radiation and injury), a prolonged increase in T secretion may induce and promote the development of thyroid carcinomas. Rat thyroid tumors were compared for characteristics in common with thyroid carcinomas in man. The rat tumors had similar well-differentiated structure, slow growth, moderate invasiveness and a tendency to metastasize, metabolism of iodine, and low toxic effect on the hosts. Biological changes in the host were used to test tumor activity (adaptive potentials) and to examine the mechanisms by which environmental factors (such as iodine deficiency, thyroidectomy, gonadal, thyroid and pituitary hormones) stimulate, oppose, prevent or reverse the effect of

ic determinants on tumor growth and function. Results showed that similar factors operate in the development, prevention and therapy of thyroid carcinomas.

267 GROWTH OF TRANSPLANTABLE MAMMARY CARCINOMA IN MICE: DEPENDENCE ON AN HORMONES FOR ENHANCING EFFECT OF GROWTH AND PROLACTIN. (Heb.) Speiser, Z. (S. S. Res. Inst., Tel Aviv, Israel) and S. Gitter. Harefuah 77(9):381-384,

orectomized (oox.) mice of the R III and C57BL strains and normal and orchiectomized (orx.) males of both strains were examined for the enhancing effect of bovine growth hormone (BGH) and sheep prolactin on the growth of 2 transplantable mammary adenocarcinomas (MMC1A and Eo771). Oox. was performed 1 week prior to, or 4 days after, tumor implantation. Oox. mice were tested with or without substitution therapy of estradiol benzoate or progesterone while normal and orx. males were tested with or without testosterone propionate or estradiol benzoate. Neither BGH nor prolactin had any effect on tumor growth when ovaries were intact, in contrast to reestablishment of the enhancing effect in oox. mice given substitution therapy. Those mice receiving prolonged treatment with estradiol exhibited the greatest tumor-enhancing effect. Since males (both normal and orx.) were less sensitive to BGH, larger doses of BGH were needed, as well as greater amounts of substitution therapy, for enhancement of tumor growth.

268 HAIR LOSS IN OVARIAN TUMORIGENIC MICE. (E.) Davis, R. H. (Hahnemann Univ. Coll. Hosp., Philadelphia, Pa.), L. McGowan and P. Ryan. Proc. Soc. Exp. Biol. Med. 135(4):434-436, 1970.

Female mice of the C3B6F-W strain were selected for hair loss (rated 0-4 for no loss to 4 for loss over the entire body, resp.) and for tumors. Mice included the following genotypes: black-eyed white (BEW; genotype W^xW^y sterile, ovarian tumor-bearing mice); all-tail agoute; white-tipped tail agoute; and black tail agoute (agoute mice were the controls). Mice of all genotypes began to lose hair at 2 mo., at which time the BEW ovaries began to show branching clefts from the germinal epithelium. The mice with no hair loss for 7-9 mo. were heavier than bald ones. There was no significant difference between body size in controls and BEW mice. Greatest and least hair loss were both seen in agoute control groups (26.8% and 2.8%, resp.). The highest av. hair loss (about 1.33) was seen for tumor-bearing mice. Hair loss in controls was limited predominantly to the face, as opposed to widespread loss (face, chest, abdomen, shoulders) in tumor-bearing mice. It is concluded that both ovarian

tumorigenesis and genetic factors are responsible for hair loss, while body wt. loss appears to be an associated variable. The role of decreased estrogen secretion and gonadotropin overproduction in the etiology of tumor formation and hair loss is briefly discussed.

70-2269 MORPHOLOGY AND ENZYME HISTOCHEMISTRY OF EXPERIMENTAL TUMORS OF THE CENTRAL NERVOUS SYSTEM IN RATS. I. MORPHOLOGIC FINDINGS. (Ger.) Stavrou, D. (U. Munich Sch. Vet. Med., Germany). Acta Neuropath. (Berlin) 15(3):220-230, 1970.

Phenyldimethyltriazen (PDT; 50 mg/kg/week; s.c., mean dose 445 mg) induced 101 neurogenic tumors in 80 adult, Sprague-Dawley rats, with a mean latent period of 185 days, including 42 tumors of the brain, 3 of the spinal cord and 56 of the peripheral nerves. Admin. of N-methyl-N-nitrosourea (MNU; 6 mg/kg/dose, p.o. 2 admin./week; mean dose of 340 mg) induced 80 neurogenic tumors in 80 rats of the same strain, with a mean latent period of 430 days including 65 tumors of the brain, 6 of the spinal cord and 9 of the peripheral nerves. The 116 tumors of the central nervous system (total for both groups) included 5 sarcomas, 7 ependymomas, 8 astrocytomas, 21 oligodendrogliomas, 48 primary heteromorphic gliomas and 27 polymorphic gliomas. It is concluded that PDT displayed a greater affinity for the peripheral nervous system than was displayed by MNU.

70-2270 MORPHOLOGY AND ENZYME HISTOCHEMISTRY OF EXPERIMENTAL TUMORS OF THE CENTRAL NERVOUS SYSTEM IN RATS. II. ENZYME HISTOCHEMICAL FINDINGS. (Ger.) Stavrou, D. (U. Munich Sch. Vet. Med., Germany). Acta Neuropath. (Berlin) 15(3):231-239, 1970.

Experimental, primary iso- and heteromorphic gliomas, polymorphic gliomas and ependymomas, induced in rats, were studied in terms of the activity and distribution patterns of various hydrolases and oxidoreductases such as glucose-6-phosphate dehydrogenase, acetylcholinesterase, adenosine triphosphatase and others. Isomorphic gliomas (oligodendrogliomas, types I and II) and astrocytomas, types I and II showed a characteristic distribution pattern in terms of most hydrolases and oxidoreductases, with significantly more capillaries which were positive for alkaline phosphatase (ALP); polymorphic gliomas showed highly variable and irregular hydrolytic and oxidative enzyme patterns, with reduced ALP activity; ependymomas were strongly ALP-positive. It is concluded that these findings were strikingly similar to those made in histochemical studies of human brain tumors.

70-2271 HISTOCHEMICAL COMPARISON OF THE EFFECTS OF A CARCINOGENIC AND A NON-CARCINOGENIC

DERIVATIVE OF TRICYCLOQUINAZOLINE. (E.) Diengdoh, J. V. (St. John's Hosp. Dis. Skin Inst. Derm., London) R. W. Baldwin and J. Chayen. Brit. J. Derm. 82(1):23-26, 1970.

Staining for DNA, sulfhydryl groups, S-S-groups, and enzymes was performed on the epidermis of albino mice of the Schofield strain 24 hours and 2, 4, 6 and 8 days after a single application of 3-methyltricycloquinazoline (3-MTCQ; 1 mg/ml) or 2-methyltricycloquinazoline (2-MTCQ) in benzene soln. to the skin. The carcinogen 3-MTCQ enhanced DNA staining in the basal cells after 2 days, appreciably reduced cytochrome oxidase activity after 6 days and increased staining for sulfhydryl groups while reducing the intensity of staining for -S-S- groups, particularly in the keratin layer, as early as 24 hours after application. Noncarcinogenic 2-MTCQ produced none of these changes. Neither compound had any effect on succinate dehydrogenase activity. The activities of lactate and α -glycerophosphate dehydrogenases fluctuated with time after application, but no clear-cut correlation with the carcinogenicity of the substance applied was seen. The increased activities of phosphogluconate dehydrogenase and decreased activities of cytochrome oxidase, which were observed after painting with 3-MTCQ, apparently indicated that a single application of this substance may induce an initiated state in which the basal metabolic pattern has changed to resemble what is eventually found in fully-developed cancer.

70-2272 CARCINOGENIC PROPERTIES OF SYMMETRICAL TRIAZINE DERIVATIVES. (Rus.) Pliss, G. B. (N. N. Petrov. Sci. Res. Inst. Oncol., Leningrad, USSR) and M. A. Zabezhinskiĭ. Vop. Onkol. 16(1):82-85, 1970.

Tests run on 201 white male and female noninbred rats and on 300 male and female CC57 white mice by p.o. and s.c. admin. and skin painting showed that Simazine (2-chloro-3,6-bis(ethylamino)-s-triazine) and cyanuric acid (s-triazine-2,4,6-triol) have an insignificant carcinogenic effect. Simazine is employed in weed control and cyanuric acid is used in dye synthesis. These triazine derivatives, suspended in sunflower seed oil were admin. s.c. (1 admin./week) or p.o. (5 admin./week), or 2-3 drops of a 20% benzene soln. (3 admin./week) were applied to the skin. Max. doses of cyanuric acid were 6.06 g s.c. and 18.42 g p.o. for rats; mice were given 0.6 g s.c. and 3.24 g p.o. Max. doses of Simazine were 3.96 g s.c. and 20.58 g p.o. for rats; mice were given 0.96 g s.c. and 3 g p.o. In skin tests, mice were given 3.45 g cyanuric acid or 3.74 g Simazine; total doses for rats are not specified. Tumors never developed in more than 30% of the animals, and the av. latent period was 1.5 yr. Cyanuric acid produced the largest number of tumors when it was inj. s.c. and Simazine

when it was admin. p.o. The most common site of tumor formation was the liver (5 cases) with cyanuric acid and the forestomach (2 cases) with Simazine. The carcinogenic activity of Simazine was attributed to its chlorine atom; it was a much weaker carcinogen than cyanuric chloride (2,4,6-trichloro-s-triazine), with 3 chlorine atoms.

70-2273 MORPHOLOGICAL AND HISTOCHEMICAL STUDIES DURING 1,2-DIMETHYLHYDRAZINE (DMH) CARCINOGENESIS OF THE RAT INTESTINAL MUCOSA. (Ger.) Schauer, A. (U. Munich Path. Inst., Germany), T. Völlnagel and F. Wildanger. Verh. Deutsch. Ges. Path. 53:234-236, 1969.

Admin. of 1,2-dimethylhydrazine (DMH; 10 mg/kg/week x 24 weeks, s.c.) induced 201 tumors in 92/100 Sprague-Dawley rats. Admin. of 10-80 mg/kg/week, before and during pregnancy, induced no tumors in 120 offspring (of 40 treated animals), observed for up to 600 days. In fully developed adenomatous polyps of the small intestine, both acid and alkaline phosphatase levels were severely reduced, with only scattered, small foci of activity demonstrable. In adenomatous tumors of the colon, a similar loss of nonspecific esterase activity alternated with sharply increased foci of activity, sometimes within the same gland, with increased activity apparently due to the presence of regenerating cells in the crypt areas. Mitochondrial succinic dehydrogenase activity was highly variable, depending on the degree of glandular differentiation. Autoradiographic studies showed no generalized increase of incorporation of ^3H -thymidine into DNA, as compared to controls. However, a significant increase of such incorporation was shown in band-like, rapidly growing areas at the surface of fully developed adenomatous and villous tumors. In general, all the benign and malignant intestinal tumors found in man were demonstrable in these animals. No synergism between DMH and X-irradiation was noted.

70-2274 TRANSFORMATION OF CELLS BY 6-CARBOXY-4-NITROQUINOLINE-1-OXIDE. (Jap.) Moriyama, Y. (Nippon Med. Sch., Tokyo). J. Nippon Med. Sch. 36(6):425-433, 1969.

Embryonal hamster cells were cultured in a medium containing 6-carboxy-4-nitroquinoline 1-oxide at a conc. of 1×10^{-5} M. After day 8, the cells became large, squamous and vacuolized; cellular infiltration was noted by 30 days. When these cells were inoc. into hamsters, 2/3 developed tumors and died in 56 days. Histologically, the tumors were spindle cell carcinomas.

70-2275 INCORPORATION OF CARCINOGENIC NITROQUINOLINE 1-OXIDE DERIVATIVES INTO CYTOPLASMIC PROTEIN OF Tetrahymena. (E.) Mita,

Nat. Cancer Ctr. Res. Inst., Chuo-ku, Tokyo),
unakata and W. Nakahara. Exp. Cell Res.
0:299-301, 1970.

ures of Tetrahymena pyriformis incorporated
-nitroquinoline 1-oxide (NQO) very rapidly
a peak by 60 min. Sucrose density gradient
rifugation showed labeled NQO in the top frac-
s for the cytoplasm; low incorporation was seen
the nucleus, with none seen in the ribo-
s. It is concluded that NQO has no affinity
RNA and that ribosomes are not the target
the carcinogenic action of NQO. The
ibility of an interaction of cytoplasmic
ein with NQO in the mechanism of induction
omalies of Tetrahymena is suggested.

276 INTERACTION OF 4-NITROQUINOLINE 1-
OXIDE WITH DEOXYRIBONUCLEIC ACID AND
METIC POLYDEOXYRIBONUCLEOTIDES. (E.) Paul,
(U. Texas Southwestern Med. Sch., Dallas)
P. O. Montgomery, Jr. Molec. Pharmacol.
315-322, 1970.

d upon difference spectral analysis, the
deoxyribonucleotide, deoxyguanosine:deoxy-
idine (dG:dC), exhibited less interaction
4-nitroquinoline 1-oxide (NQO) than did
ve calf thymus DNA, while polydeoxy(adenosine-
idine) or denatured calf thymus DNA caused
minor interaction. Addition of sodium
ride (0.5 mM to 1.0 M) decreased the
ct of native DNA on the difference spectrum
QO by about 400%. This interaction was
ly dependent on ionic parameters, indicating
ges sites in the interaction of NQO and DNA.
tion of urea (6 M) abolished the effect of
on the difference spectrum of NQO, possibly
cating some role of hydrogen bonding in
formation of the DNA-NQO complex or the
ration of hydrophobic interactions resulting
isruption of this complex. Addition of
significantly stabilized strand separation
ative DNA. Examination of the binding of
ve DNA with NQO revealed a nonlinear curve
istent with the involvement of more than
teraction site in the formation of the
lex. An intact double-helical conformation
A and guanosine-cytidine pairs were essential
max. complex formation.

277 ELECTRONIC PROPERTIES OF N-HETEROARO-
MATICS. XI. CHARGE-TRANSFER INTER-
NS OF THE CARCINOGEN 4-NITROQUINOLINE 1-
WITH METHYLSUBSTITUTED BENZENES AND
LSUBSTITUTED ANILINE DERIVATIVES. (Jap).
, T. (Tohoku U. Pharmaceut. Inst., Sendai,
, T. Miura, M. Yoshida and K. Uekama.
aki Zasshi (J. Pharm. Soc. Jap.) 89(10):
1385, 1969.

rophotometric analysis of 4-nitroquinoline
de (NQO) and its interaction with methyl-
ituted benzenes and aniline derivatives

showed a 1:1 molar ratio for complexes formed
and a shift of absorption bands to longer wave-
length with increased solvent polarity; analysis
of pH effect favored interaction by the unionized
aniline derivatives. It is concluded that
 π - π type and n - π type charge transfers are
involved, and that in the interaction studied
NQO is a stronger π -acceptor than the non-
carcinogen 4-nitropyridine 1-oxide.

70-2278 AN INVESTIGATION INTO THE POSSIBLE
PRESENCE OF NITROSAMINES IN NITRITE-
BEARING SPINACH. (E.) Keybets, M. J. H. (Agric.
Univ., Wageningen, Netherlands), E. H. Groot
and G. H. M. Keller. Food Cosmet. Toxic. 8(2):
167-171, 1970.

Spinach containing no demonstrable nitrite was
stored under such conditions as to increase the
nitrite conc. to 251 and 78 ppm after 1 week at
20-23° C and 2 weeks at 4° C, resp. Extraction
of nitrosamines and thin-layer chromatography
showed no nitrosamines in stored spinach or
spinach treated with excess diethylamine and
stored or heated for 1 hour at 70-80° C.
Lowering the pH from 10.1 to 3.1, followed by
1 week of storage, resulted in the presence
of some diethylnitrosamine (0.45% of the possible
amount). Spinach with higher nitrite conc.,
which was stored or heated, also showed some
nitrosamines. It is concluded that the weakly
alkaline reaction of spinach and the low conc.
of secondary amines are limiting factors in
the synthesis of nitrosamines by spinach.

70-2279 DIMETHYLNITROSAMINE-INDUCED HEPATIC
CIRRHOSIS: A NEW CANINE MODEL OF AN
ANCIENT HUMAN DISEASE. (E.) Madden, J. W.
(U. Arizona Coll. Med., Tucson), P. M. Gertman
and E. E. Peacock, Jr. Surgery 68(1):260-268,
1970.

Hepatic cirrhosis developed in 5/8 mongrel dogs
admin. dimethylnitrosamine (DMNA; 2.5 μ liters/kg;
2 admin./week x 4 weeks, p.o.) and 3/8 developed
transient cellular changes that improved with
time. Each of the 5 cirrhotic animals
developed significantly increased hepatic hydroxy-
proline conc. compared to the unchanged collagen
conc. in noncirrhotic dogs. All cirrhotic
animals developed significant elevations in
portal pressure and all 8 animals demonstrated
at least some spontaneous portosystematic shunting.
Intractable ascites developed in 3/5 cirrhotic
dogs. It is suggested that this model may be
useful in the study of other parameters of
hepatic cirrhosis.

70-2280 HISTOGENESIS AND MORPHOGENESIS OF
EXPERIMENTAL KIDNEY TUMORS IN ANIMALS.
(Rus.) Benemanskii, V. V. (Ministry Health Inst.
Biophys.; Moscow) and N. N. Litvinov. Ark. Pat.
31(10):79-84, 1969.

A histological and histochemical study was made of kidney tumors induced in 107/312 adult male albino rats by p.o. admin. of dimethylnitrosamine (2 doses of 15-20 mg/kg, 20 days apart, or 105 doses of 3 mg/kg over 4 mo. The 156 tumors found at autopsy consisted of 36 benign cystadenomas, 23 tubular adenomas, 14 alveolar basophilic-cell adenomas, 15 alveolar clear-cell adenomas, 4 adenocarcinomas, 11 tubular carcinomas, 2 solid polymorphocellular tumors, 6 clear cell carcinomas resembling Grawitz's tumor in man, 39 anaplastic tumors resembling Wilms' tumor in man and 6 sarcomas. By following precancerous changes it was demonstrated that tumors developed from foci of hyperplastic, rapidly proliferating cells and were associated with dystrophic and regenerative processes. Adenomas, cystadenomas and cysts originated from the epithelium of the convoluted tubules in the proximal part of the nephron and, more rarely, from the epithelium of the external layer of Bowman's capsule. Malignant epithelial tumors developed indirectly from benign tumors or directly from the proliferating renal epithelium. Clear cell carcinomas of the Grawitz type developed from the epithelium of the convoluted tubules indirectly from clear cell adenomas. Anaplastic tumors originated from undifferentiated and cambium cells in the intertubular spaces. No significant differences were found in the activities of succinate dehydrogenase, NAD and NADP diaphorase, and lactate dehydrogenase in precancerous tissue and the surrounding normal tissue.

70-2281 N-METHYL-N'-NITRO-N-NITROSOGUANIDINE: REACTIONS OF POSSIBLE SIGNIFICANCE TO BIOLOGICAL ACTIVITY WITH MAMMALIAN CELLS. (E.) Anderson, T. J. (Roy. Infirm., Glasgow, Scotland) and R. H. Burdon. *Cancer Res.* 30(6):1773-1981, 1970.

By determining incorporation of ^3H -labeled thymidine, uridine, and deoxyadenosine and ^{14}C -labeled amino acids it was demonstrated that DNA, RNA and protein synthesis were immediately inhibited in hamster fibroblasts exposed to N-methyl-N'-nitro-N-nitrosoguanidine (MNNG). DNA synthesis was the most sensitive to inhibition and showed a dose-dependent relationship. Both purine and pyrimidine incorporation were altered. Inhibition of DNA synthesis was not due to impaired uptake or phosphorylation of the precursors but to dose-dependent inhibition of DNA polymerase by MNNG. Experiments with exogenous thiols indicate that thiol groups of DNA polymerase may be targets for reaction with the guanidino radical resulting from MNNG decomposition. Further studies suggest that thiol and other groups possibly involved in substrate binding may be altered and that enzyme kinetics favor a mixed mode of inhibition.

70-2282 EFFECT OF VARIOUS DOSES OF N-NITROSOMETHYLUREA AND N-NITROSOETHYLUREA

ON THE DEVELOPMENT OF SPONTANEOUS LEUKEMIA AND TUMORS IN MICE. (Rus.) Martynova, R. P. (Inst. Cytol. Genet., Novosibirsk, USSR), G. M. Ronichevskaya and B. A. Sekirov. *Vop Onkol.* 15(6):53-56, 1969.

On day 20 of gestation, pregnant mice belonging to the leukemia-susceptible AKR line were exposed for 24 hours to inhalation of small doses (0.8 g) of N-nitrosomethylurea. Their 42 offspring were exposed to the same dose 8 days later. Frequency of leukemia among these mice was significantly lower (45%) than among 56 control mice of the same age and sex (69%). The mean lifespan was significantly longer in the experimental group (about 17 mo.) than in the controls (about 10.7 mo.). Large doses (total doses of 55 mg) of N-nitrosoethylurea, injected s.c. into line A mice over a 2 mo. period, produced tumors (4 thymomas and 1 mammary gland tumor) in 5/17 surviving females; no tumors developed in the controls.

70-2283 HISTOCHEMICAL EVALUATION OF HYDROLYTIC ENZYMES IN TUMORS INDUCED IN THE RAT BY NITROSOUREA DERIVATIVES. (E.) Fabiani, A., D. Schiffer (U. Turin Clin. Dis. Nen. Syst., Italy), P. Paoletti and E. Grossi-Paoletti. *Acta Neuropath.* (Berlin) 15(3):272-278, 1970.

Tissues of 34 experimental tumors (neurinomas and gliomas; 25/34 were tumors of the nervous system obtained in rats by a 10 mg/kg body wt. dose of nitrosoethylurea given to the mother on day 17 of gestation; 9/34 were from rats admin. 25 mg/kg nitrosomethylurea/mo.) were examined for enzymatic activity. The neurinomas showed very low acid phosphatase (AP) activity in the florid areas, and foci of AP only in scattered cells. In these cells the activity was located lateral to the nucleus and had a granular shape. E 600-resistant naphthol esterase and β -glucuronidase had the same distribution pattern. In regressive areas with colligation, spongiosis and cyst formation, the AP activity was greatly increased; it was very intense in areas of necrosis. AP activity was evident in only a few elements of the cystic wall in areas of complete tissue colligation; β -glucuronidase and E 600-resistant esterase showed the same pattern. In the gliomas, AP activity was scarce in isomorphous areas and intense in polymorphous areas. E 600-resistant esterase and β -glucuronidase again showed the same pattern, while E 600-sensitive esterase gave a diffuse reaction. Indoxylesterase had the same distribution as naphthylesterase after E 600; alkaline phosphatase was limited to the vascular network. The findings are compared with those for human tumors.

70-2284 MORE ABOUT THE INDUCTION OF BRAIN TUMORS IN RATS WITH METHYLNITROSOUREA. (Rus.) Dimant, I. N. (Sci. Res. Inst. Roentgen. Radiol. Oncol., Tashkent, USSR), G. M. Loktionov, M. M.

aeav and A. A. Israilian. Biull. Eksp. Biol.
1. 69(5):90-92, 1970.

female noninbred rats, exposure of the ovaries
X-irradiation (dose unspecified) had no
significant effect on the induction of brain
tumors by i.v. inj. of methylnitrosourea (MNU;
dose unspecified) if all of the animals were
considered. However, autopsy examinations
showed that radiation exposure had induced
ovarian cysts and, consequently, hyperestrogenism,
6/9 surviving rats, 5/6 of which developed
brain tumors. The results indicated a signifi-
cant correlation between hormone imbalance and
the development of MNU-induced brain tumors.
The feeding of 6-methylthiouracil, which also
caused hormone imbalance, enhanced tumor
development in MNU-treated rats.

2285 THE EFFECT OF PARTIAL HEPATECTOMY ON
THE METABOLISM OF URETHAN IN YOUNG
BALB/c MICE. (E.) Grogan, D. E., M. Lane
Baylor Coll. Med., Houston, Tex.), R. A. Liebelt
and F. E. Smith. Cancer Res. 30(6):1806-1811,
1970.

Results from previous investigations and study
of ¹⁴C-carbonyl urethan metabolism in 8-10-week-
old male and female BALB/c/Ki mice support the
view that the increased rate of cell prolifera-
tion after partial (70%) hepatectomy (hpx.) en-
hances the susceptibility of the liver to the
carcinogenic effect of urethan. Urethan conc.
in whole blood and liver and in liver subcellular
fractions, RNA and DNA were essentially the same
in intact and partially hpx. mice. No radio-
activity was detected in the blood or liver
of intact or operated mice 24 hours after each
3 inj. of ¹⁴C-labeled urethan (1 mg/g body
wt., route unspecified) given on alternate days.

2286 EFFECT OF PARTIAL HEPATECTOMY ON TUMOR
INCIDENCE IN BALB/c MICE TREATED WITH
URETHAN. (E.) Lane, M. (Baylor Coll. Med.,
Houston, Tex.), A. Liebelt, J. Calvert and R. A.
Liebelt. Cancer Res. 30(6):1812-1816, 1970.

The frequency of hepatomas in male and female
BALB/c/Ki mice, 8-10-weeks-old, suggested that
the increased rate of liver cell proliferation
after partial (30% or 70%) hepatectomy (hpx.)
enhance the susceptibility of the liver to the
carcinogenic action of urethan (U.).
The enhancement of the carcinogenic activity of
U. in hpx. mice may result from the conc. of
regenerating liver cells to a greater
extent than by resting cells, or a decrease
in the rate of elimination of U. from the liver,
or that tissues are more exposed to the carci-
nogen. U. was inj. i.p. on alternate days (3
times of 1 mg/g body wt. each). In operated
mice, U. inj. was begun 2 days after partial hpx.
The frequency of lung tumors was significantly

higher in all U-treated groups than in untreated
controls, but the frequency of hepatomas was in-
creased only in 70%-hpx. U-treated mice. The
mitotic index was significantly higher in 70%-
hpx. males than in sham-operated mice or in 30%-
hpx. animals. A significant difference in the
mitotic index of liver tissue was seen between
males and females in the 70%-hpx. groups, the
mitotic index being higher in males than in fe-
males. The frequency of leukemia was significantly
lower in all U-treated mice; this finding could
not be explained.

70-2287 POSTNATAL CELLULAR PROLIFERATION IN
MOUSE AND HAMSTER LUNG. (E.) Crocker,
T. T. (U. California Cancer Res. Inst., San
Francisco), A. Teeter and B. Nielson. Cancer
Res. 30(2):357-361, 1970.

Syrian hamsters and strain A mice (0-28 days old)
were inj. with ³H-thymidine (10 µCi; i.p.) 1 hour
before sacrifice. Spectrometric analysis of
portions of mouse lung tissue showed a low
amount of labeled cells in mice 0-1 day old, with
about a 10-fold increase by day 3 persisting
to day 8, and then a decline by day 14 to
levels seen at birth. A similar pattern was
seen for hamster lung, but the decline occurred
at age 6 days. The wt. of hamster lung increased
about 3-fold from 0-3 days, leveled off, and then
increased with body wt. It is suggested that
tumorigenesis and max. proliferation are re-
lated to similar processes observed in urethan-
treated, genetically predisposed adult mice.

70-2288 CARCINOGENICITY OF URETHAN AND MYE-
LOGENOUS CHLOROBLASTIC VIRUS IN ADULT
MICE. (Rus.) Stromskaia, T. P. (Inst. Exp.
Clin. Oncol., Moscow). Vop. Onkol. 16(2):
63-65, 1970.

Frequency of leukemia was low in male and
female CBA-T6T6 mice (aged 2-4 mo.), inj. i.p.
with 0.1 ml of a 10% extract of a myeloid
chloroblastic virus (obtained from leukemic
mice) and i.p. with urethan (U; 1 mg/g body wt.;
4 admin. at 3-4 day intervals), either separately
or in combination. The frequency of pulmonary
adenomas, which ranged from 50.0-76.1% in U-
treated animals, was only 8.5% in virus-infected
mice; none of the controls developed pulmonary
adenomas. Hepatomas were found in all of the
experimental groups, but their frequency was
lowest in animals receiving both virus and
U; this was explained by the small number of
animals used in this experiment, and the
smaller proportion of males in groups receiving
both virus and U.

70-2289 CYTOTOXIC AND MUTAGENIC ACTIVATION
OF URETHANE BY N-HYDROXYLATION AND
O-ESTERIFICATION. (E.) Fahmy, O. G. (Chester
Beatty Res. Inst. Cancer Res., London) and

M. J. Fahmy. Chem. Biol. Interactions 1(3): 257-270, 1969/70.

The cytotoxic and mutagenic activities of urethan (U) and its metabolites, N-hydroxyurethan (HU) and N,O-diacetyl-N-hydroxyurethan (DAHU), were investigated in the testis of adult *Drosophila melanogaster*. Crossing-over experiments and the variations in sterility among progeny fractions of the treated males showed that all 3 compounds had a cytotoxic effect on the germ cells. U and HU affected only the metabolically active earlier presperm stages (spermatids, spermatocytes and spermatogonia). DAHU acted on all stages of spermatogenesis; its greatest effect, however, was on metabolically inert mature sperm. It is indicated that cytotoxicity, especially that of DAHU, did not result from viable chromosome rearrangements, but may have been caused by induction of open chromosome breaks leading to dominant lethals. Point-mutations (recessive visibles and lethals) occurred only when U, HU and DAHU were admin. in massive and highly toxic doses. These mutations occurred preferentially in mature sperm: all 3 compounds had very little effect on early germ cells. The frequency with which DAHU produced point-mutations was slightly higher than that of the other 2 compounds. U and HU both induced small chromosome deletions in the early stages of spermatogenesis, but DAHU was much more effective in this respect and also acted on mature sperm. These deletions are probably due to the inhibitory action of U and its metabolites on DNA synthesis. DAHU or some related amino-oxy ester probably produces the small chromosome deletions which are considered to be the genetic aberration involved in U carcinogenesis. None of the compounds induced viable chromosome rearrangements.

70-2290 EFFECT OF URETHAN AND N-HYDROXYURETHAN ON ORGAN CULTURES OF EMBRYONIC MOUSE LUNG TISSUE. (Rus.) Kolesnichenko, T. S. (Inst. Clin. Exp. Oncol., Moscow). Vop. Onkol. 16(1):112-114, 1970.

A comparison of the effects of urethan (U) and N-hydroxyurethan (OH-U) on cultures of lung fragments from 18-20-day-old embryos of mouse line A revealed that OH-U had a considerably stronger cytotoxic effect than U at the same conc. Neither compound had any effect at a conc. of 0.25 mg/ml, but at higher conc. (0.5, 1.0, and 2.0 mg/ml) both compounds produced dystrophic changes, the extent of which increased with conc. At a conc. of 0.5 mg/ml, OH-U caused partial necrosis in some of the cultures after 17-21 days of incubation; no necrosis was seen with the same conc. of U. At a conc. of 1.0 mg/ml, OH-U induced partial necrosis after 11 days and complete necrosis after 14 days; U also caused necrosis, but to a

lesser extent and after longer incubation. These findings neither support nor refute the hypothesis that the tumorigenic effect of U is due to its metabolite, OH-U.

70-2291 EFFECT OF INFLUENZA VIRUS ON EXPERIMENTAL CARCINOGENESIS. (Rus.) Frolov, A. F. (Inst. Epidem. Microbiol. Parastitol., Kiev, USSR). Vop. Onkol. 16(5):72-76, 1970.

Experiments with male and female CC57W mice, which are highly susceptible to lung tumors, and male and female noninbred mice, all aged 2-3 mo., showed that mice given 120 mg urethan (0.75 mg/g body wt. s.c. every 7 days for 3 mo.) and type A₂ or B influenza virus (3 intranasal instillations of 5×10^3 - 10^4 ID₅₀, each at 2 week intervals) developed significantly more tumors, particularly lung tumors, than mice given urethan alone or influenza virus alone. Pulmonary adenomas were the most prevalent histological form of lung tumor in all three of these groups. However, the frequency of lung cancer and precancer was higher among mice given both urethan and influenza virus. Lymphomas were more common in mice given influenza virus alone than in those given both urethan and influenza virus. The frequency of tumors other than those of the lung was higher in both CC57W and noninbred mice given both urethan and influenza virus than in the other groups; this was most marked among CC57W mice. These included cancer of the liver in 3 and of the maxillary gland in 3; only 1 mouse given urethan alone developed any cancer (submaxillary gland cancer). The higher frequency of tumors in noninbred mice given both urethan and influenza virus was due primarily to a higher frequency of mammary gland tumors.

70-2292 SERUM ESTERASES AND AFLATOXIN. (Fr.) Monjour, L. (African Org. Res. Food Nutr., Dakar, Senegal) and C. Mariage. C. R. Soc. Biol. (Paris) 163(5):1261-1265, 1969.

Male, adult Wistar Commentary rats were fed a diet containing aflatoxin (0.75 mg/kg food), and the properties of serum esterases were studied by gel electrophoresis on polyacrylamide agar. Aflatoxin-fed rats with liver carcinomas lost part (73%) of the C fraction (α -globulins) esterases, possibly during the course of malignant transformation. It is suggested that aflatoxin is a partial inhibitor of protein biosynthesis.

70-2293 EFFECT OF INGESTION OF AFLATOXIN ON PROTEIN SYNTHESIS IN RATS. THE PROBLEM OF NEOANTIGENS. (Fr.) Monjour, L. (African, Org. Res. Food Nutr. Dakar, Senegal) and C. Mariage. C. R. Soc. Biol. (Paris) 163(5): 1251-1254, 1969.

le Wistar Commentry rats were fed impure aflatoxin (A; 0.75 mg/kg of feed) derived from Aspergillus flavus. Sera from A-treated rats showed no embryonic antigen. Rabbits of a common strain were immunized by a serum pool from 14-mo.-old rats fed A since weaning. A coat antigen, characteristic of those found during hepatic regeneration and development of liver tumors, was detected in the rat sera. It had an immunoelectrophoretic mobility of a β -protein and did not stain as glycoprotein.

2294 METABOLISM OF AFLATOXIN IN SUSCEPTIBLE AND RESISTANT ANIMAL SPECIES. (E.) Peterson, D. S. P. (Cent. Vet. Lab., New Haw, Surrey, England) and R. Allcroft. Food Cosmet. Toxicol. 8(1):43-53, 1970.

Aflatoxin B₁ (AB) was admin. to various species of animals. AB was excreted either unchanged as aflatoxin M₁ (AM) by rats, goats and guinea pigs, but possibly not by mice and ducklings. The AM-conjugated form was excreted only by guinea pigs. When AB was admin. i.p. to chicks and ducklings, within 10-60 min. AM was found in the kidneys of ducklings. Neither species had AB or AM in the liver after 30 min.; after 60 min., some AB was seen in chick tissues. Other aflatoxin metabolite (termed metabolite X) was found after metabolism *in vitro* by liver homogenates; as the AB conc. increased. In chicks, liver metabolism of AB *in vitro* remained unaffected by increasing age.

2295 HISTOCHEMICAL STUDIES ON THE ACTION OF AFLATOXINS. II. A CYTOLOGICAL STUDY OF LIVER OF RATS FED A DIET CONTAMINATED WITH Aspergillus parasiticus. (E.) Miętkiewski, (Med. Acad., Poznan, Poland), J. Janicki, L. Wondowicz, M. Urbanowicz and B. Filipiak. Acta Histochem. Cytochem. (Krakow) 8(1):47-58, 1970.

Albino Wistar rats were admin. Aspergillus parasiticus (Apara; 0.0625 mg aflatoxin B₁/day in the diet) and results after 10 and 18 days compared to changes produced in rats fed A. flavus (Aflav) in previous experiments. Significant changes in the liver, such as proliferation of biliary canaliculi and hepatic necrosis, were seen by day 10, as well as a decrease in glycogen content in transforming hepatocytes. By day 18, changes were even greater for the Apara group and no glycogen reaction was found in the lobule (for Aflav it was still present after 23 days). Although observed changes were less with Apara than with Aflav, the quantity of aflatoxins was also less in this experiment. It is concluded that the effects of aflatoxins in the diet of rats were similar to those of Aflav, except for the lack of glycogen reaction by day 18 with the former.

70-2296 OCCURRENCE OF AFLATOXIN AND Aspergillus IN FOODS. (Fr.) Boutibonnes, P. (Microbiol. Lab., Caen, France) and J. Jacquet. C. R. Soc. Biol. (Paris) 163(5):1119-1124, 1969.

The conc. of aflatoxin and presence of spores of Aspergillus, especially A. flavus, were determined for 400 samples of foods or animal feeds, obtained mostly from the region of Paris and Caen, France. Spores were commonly found on grains, fruits and even shrimp cakes; they were found more often on products of tropical origin (especially from Africa) than on foods from temperate climates. Although the amount of aflatoxin was generally very small, some animal feeds (peanut cakes and meal) had conc. up to 4.5 mg/kg. The importance of differentiating the presence of spores which may never germinate from those which are toxigenic and from the presence of aflatoxins in food products, is stressed.

70-2297 AFLATOXICOL: STRUCTURE OF A NEW TRANSFORMATION PRODUCT OF AFLATOXIN B₁. (E.) Detroy, R. W. (Northern Reg. Res. Lab., Peoria, Ill.) and C. W. Hesseltine. Canad. J. Biochem. 48(7):830-832, 1970.

Incubation of aflatoxin B₁ with strain NRRL2575 of Dactylium dendroides, a steroid-hydroxylating fungus, yielded aflatoxicol. In contrast to the parent compound, aflatoxicol lacked infrared absorption bands for coumarin and ketone functions but appeared to contain a reduced carbonyl group in the cyclopentane ring. Its molecular formula, obtained by mass spectrometry, indicates aflatoxicol is a dihydro derivative of aflatoxin B₁.

70-2298 THE ACUTE TOXICITY OF RETRORSINE, AFLATOXIN AND STERIGMATOCYSTIN IN VERVET MONKEYS. (E.) Van Der Watt, J. J. (South African Med. Res. Council, Pretoria) and I. F. H. Purchase. Brit. J. Exp. Path. 51(2):183-190, 1970.

The 10 day LD₅₀ values for retrorsine, aflatoxin and sterigmatocystin were 46, 3.7 and 32 mg/kg, resp., in vervet monkeys. Retrorsine was dissolved in a 50:1 mixture of water and conc. hydrochloric acid and aflatoxin was suspended in a 1.5% aqueous suspension of methyl cellulose; both of these compounds were admin. by gastric intubation. Sterigmatocystin was inj. i.p. in a dimethyl sulfoxide (DMSO) soln. All 3 compounds produced bile duct proliferation, but aflatoxin had the most pronounced effect. The LD₅₀ determined for sterigmatocystin was probably not accurate since, in contrast to other reports in the literature, DMSO produced severe fatty changes in the liver. All 3 compounds caused hepatocellular degeneration and hemorrhagic necrosis.

70-2299 MECHANISMS OF CARCINOGENESIS. (E.) Brues, A. M. (Argonne Nat. Lab., Argonne, Ill.), H. Auerbach, G. M. DeRoche and D. D. Grube. Argonne Nat. Labs. Ann. Rep. ANL-7535-28-31, 1968.

Changes in the physical configuration of implanted plastic discs (Teflon, Silastic, cellophane, Millipore filters) resulted in marked changes in rat sarcoma induction, although all materials tested produced tumors. As porosity of the Millipore filter increased from 0.1-1.0 μ , tumor production decreased, while those discs with large holes spaced 1 mm apart produced tumors; admin. of x-irradiation during the latent period failed to increase sarcoma yield. Implantation s.c. of Mylar-laminated sources containing ^{90}Sr - ^{90}Y (0.5-5.0 μC) produced capsule sarcomas more rapidly and with higher frequency than non-radioactive Mylar implants. A total of 16 discs (some radioactive) implanted in each of 5 beagles for 24-30 mo. failed to produce tumors. Preliminary results of s.c. inj. of particulate ^{239}Pu in normal and oophorectomized (oox.) female rats showed both groups had similar deposition after 170 days; the ^{239}Pu deposition in the liver of oox. rats was less than in normal rats for the 100-day period. Preliminary results with a group of 6-mo.-old female hairless mice irradiated (5000 rads total; 7.5 rads/min. from a β -emitter) and 2 weeks later painted with phorbol esters (3 admin./week) showed no tumors 100 days after initiation of skin painting.

70-2300 POLYMER TUMORIGENESIS: CLONAL DETERMINATION OF HISTOPATHOLOGICAL CHARACTERISTICS DURING EARLY PRENEOPLASIA; RELATIONSHIPS TO KARYOTYPE, MOUSE STRAIN, AND SEX. (E.) Johnson, K. H. (U. Minnesota Coll. Vet. Med., Minneapolis), L. C. Buoen, I. Brand and K. G. Brand. J. Nat. Cancer Inst. 44(4):785-793, 1970.

Histological examination of tumors induced in CBA/H and CBA/H-T6 mice by s.c. implantation of plastic films (unplasticized vinyl chloride acetate copolymer) demonstrated 4 classes of tumors: well-differentiated fibrosarcomas; spindle cell sarcomas; anaplastic round-cell sarcomas without giant cells; and anaplastic sarcomas with giant cells. Very similar morphologic characteristics were seen for homologous tumors arising from segments of the same implant transferred (6 or more mo. after initial implantation) to recipient mice during the pre-neoplastic phase. The hypothesis that a pre-neoplastic cell clone is present on the film surface soon after implantation and that homologous tumors are derived from cells of the same clone is substantiated by these results. Tumors in classes with higher anaplasticity tended strongly to tetraploidy. CBA/H mice tended to produce more anaplastic tumors than did CBA/H-T6 mice. Tumors from female mice predominated in morphologic classes with lower

anaplasticity, whereas the few tumors from male mice fell into classes with higher anaplasticity.

70-2301 COMBINED ACTION OF OPTICAL BRIGHTENERS AND ULTRAVIOLET LIGHT IN THE PRODUCTION OF TUMOURS. (E.) Bingham, E. (U. Cincinnati Coll. Med., Ohio) and H. L. Falk. Food Cosmet. Toxic. 8(2):173-176, 1970.

Male, young adult C3H mice were treated with optical brighteners, (compounds used in laundry products, fabrics and all-purpose cleaners which "brighten" the fabric). Admin. of 1 coumarin compound or 2 stilbene derivatives (50 mg of 1% soln. in dimethyl sulfoxide; 3 admin./week to the intrascapular skin) was followed by exposure to UV light (6 hours/day x 5 days/week) for some groups of mice. Mice treated with brightener alone developed no tumors, and 2 UV-treated control mice developed carcinomas. Frequency of tumors was high, however, in UV-treated mice for all substances tested. By 64-73 weeks, most of the tumors were squamous cell carcinomas. It is suggested that the mechanism of carcinogenesis involves either UV activation of the brightener or effects on the skin.

70-2302 THE EFFECT OF AGENTS ALTERING HAEMOSTASIS ON THE EVOLUTION OF TUMOURS IN MICE. (E.) Bresson, M.-L. (Paul Brousse Hosp. Inst. Cancer Immunogenet., Villejuif, France), A. Cattani and M. Hayat. Rev. Europ. Etud. Clin. Biol. 15(4):442-443, 1970.

A variety of hemostatic agents were admin. by various routes to 2 groups of mice with isogenic tumors: Group 1 consisted of C3H/eb mice previously inj. s.c. with BP8 tumor cells; Group 2 consisted of C57BL/6 mice previously inj. s.c. with 10^6 E (AKR) tumor cells. Results for Group 1 showed that calcium heparinate, epsilon amino-caproic acid and Kunitz's inhibitor caused a significant increase of tumor wt. at the inj. site. Kunitz's inhibitor significantly diminished the number of metastases. In group 2, calcium heparinate and urokinase caused a significant reduction of tumor wt. at the inj. site but increased the frequency of metastases. The effects of these compounds depended on the nature of the tumor cells inj. (the BP8 tumor was originally induced by a carcinogen; the E leukemia was originally induced by Gross leukemia virus).

70-2303 STUDIES ON A NEUROLOGICAL DISORDER AND TUMORS INDUCED BY CYCASIN IN NEWBORN NICE. (Jap.) Shibuya, C. (Gifu U. Sch. Med., Japan). Gifu Ikadaigaku Kiyo (Acta Sch. Med. Gifu) 16(4-5):479-492, 1969.

Strain dd and C57BL mice were given a single dose of cycasin (C; s.c. or p.o., 24 hours after birth) which induced cerebellar ataxia.

stological study showed extensive necrosis of the cerebellum by 72 hours after C admin. The dosage had to be doubled in dd mice for comparable symptoms to result. Reticulum cell sarcomas developed in those mice admin. within 24 hours of birth, and hepatomas developed in those surviving more than 280 days.

2304 RISK OF CANCER IN THE PRODUCTION OF ACETONE AND PHENOL (RESINS FORMED BY PYROLYSIS). (Rus.) Antonov, A. M. (Saratov Med. Inst., USSR), A. V. Arkhangel'skii, T. M. Lotareva and A. M. Lunts. Vop. Onkol. 16(5): 1-82, 1970.

With light and heavy pyrolytic resins, formed during the industrial production of acetone and phenol, were carcinogenic in skin painting tests on mice and rabbits. Heavy pyrolytic resin produced papillomas in 20/25 mice and in 6/6 rabbits. These papillomas became malignant in 20 mice and in 1/6 rabbits; the rabbit papilloma metastasized to 1 cervical lymph node. Autopsies showed that 22/25 mice had developed leukemia. Light pyrolytic resin produced papillomas in 11/29 mice and in 6/6 rabbits, with malignant transformation in 7/11 mice but 0/6 rabbits. Alkylbenzene resin produced no neoplasms in mice and caused small papillomas in 2 rabbits. None of these papillomas became malignant. The noncarcinogenic effect of this resin conflicts with another report in the literature. This difference is difficult to explain, but it might be due to differences in starting materials or in technology.

2305 COMPARATIVE EVALUATION OF THE TOXIC AND POSSIBLE CARCINOGENIC ACTION OF BENZOTRIAZOLE AND PHENIDONE (1-PHENYL-3-PYRAZOLIDONE). (Rus.) Vasil'eva, N. N. (Inst. Exp. Clin. Oncol., Moscow). Gig. Tr. Prof. Zabol. 13(3):55-56, 1970.

Studies of benzotriazole (BT), a component of the emulsion used in color movie film, and phenidone (PD), a developing agent, in rats and mice disclosed that these substances were not carcinogenic for rats, but might induce leukemia in hybrid mice. Tests were run on 315 male and female (C57BL x CBA) F₁ mice (weight 120 g) and 272 male and female Wistar and inbred rats (weight 80-90 g). BT and PD were admin. (0.1 g/kg body wt.; 1 admin./week x 5 weeks; p.o.) to mice and for 46 weeks to rats (s.c.). BT and PD were both admin. as 1% suspensions in soln. of colloidal Infusin protein species-nonspecific Belenkii's serum. Total doses were 900-1000 mg for rats and 92 mg for mice. Only 3/272 rats developed tumors (pulmonary fibroma, 1 mammary adenoma and 1 pleomorphic sarcoma originating from the mesentery). Interpretation of the findings on hybrid mice was difficult, since 55% of the untreated controls eventually developed tumors (mostly pulmonary adenomas and

hepatomas); 8.5% had malignant tumors and 3.4% had leukemia. Although the frequency of leukemia was significantly higher (13.7%) among BT-treated mice and approached statistical significance (10.7%) among PD-treated mice, 11.1% of controls inj. with solvent alone also developed leukemia. Thus, the high frequency of leukemia in treated animals may be caused by the stimulating effect of solvent on hematopoietic tissue rather than by BT or PD.

70-2306 SURGICAL ADHESIVES AND CARCINOGENESIS. PRELIMINARY STUDY. (Sp.) Just Viera, J. O., G. A. Escalera and G. H. Yeager. Bol. Asoc. Med. P. Rico 62(6):181-182, 1970.

Methyl 2-cyanoacrylate adhesives (Ethicon's Eastman 910 or Borden's Ad-here) were inj. (0.3 ml; s.c.) into groups of mice of varying sensitivity to carcinogens. Animals were sacrificed after an observation period of 6 mo. Of the mice treated with Eastman 910 which survived 6 mo., 38/116 were albino, 48/116 were C3H and 30/116 were C57. Of the mice treated with Borden Ad-here which survived 6 mo., 35/107 were albino, 28/107 were C3H and 44/107 were C57. Autopsy revealed s.c. masses in 34/337 (10%) mice, but histological examination failed to reveal a mass of the lung, liver or other suspected areas. Foreign body tissue reactions were evident in the inj. area.

70-2307 CARCINOGENICITY OF A MEDICINAL OZOKERITE AND ITS CONSTITUENTS. (Rus.) Ruchkovskii, B. S. (Sci. Res. Inst. Exp. Clin. Oncol., Kiev, USSR), Iu. P. Borisiuk and L. A. Tiktin. Vop. Onkol. 16(5):77-80, 1970.

Fluorimetric analysis and skin painting tests on mice demonstrated that ceresin (a medicinal ozokerite) contains carcinogens. In the USSR, ceresin is applied to the skin or rectal and vaginal mucosa for the treatment of a variety of diseases. Ceresin and its components were tested on 460 male non-inbred mice (aged 2-2.5 mo.) by applying either the melted substance or a 60% benzene soln. of it to the skin in 30-mg doses (2 admin./week x 10 mo.). Skin papillomas were produced after latent periods of 4.5-9 mo. by paraffin, petrolatum, heavy mineral oil and 1/2 ceresin samples. Squamous cell carcinomas of the skin were seen in 2 mice painted with mineral oil. Fluorimetric analysis of ceresin demonstrated several polycyclic hydrocarbons, identified as 3,4-benzpyrene (BP) benzo(ghi)perylene, and perylene. An aqueous extract of crude ozokerite contained traces of BP, while a benzene extract contained 70-77 µg/kg. It is recommended that petroleum products which are commonly used to improve the consistency of ceresin be analyzed for the presence of carcinogens before use.

70-2308 ULTRASTRUCTURAL AND BIOCHEMICAL CHANGES ASSOCIATED WITH PYRROLIZIDINE-INDUCED HEPATIC MEGALOCYTOSIS. (E.) Allen,

J. R. (U. Wisconsin Reg. Primate Res. Ctr., Madison), L. A. Carstens, D. H. Norback and P. M. Loh. Cancer Res. 30(6):1857-1866, 1970.

A diet containing 0.02-0.08% of ground *Crotalaria spectabilis* seed was fed to 50 male Sprague-Dawley rats for 8 mo. These seeds contain about 3.5% of the pyrrolizidine alkaloid, monocrotaline. Livers in the affected animals were composed primarily of megalohepatocytes 2.5-fold larger than normal hepatocytes, hyperplastic bile ducts and regenerative nodules. Ultrastructural and biochemical features of these affected livers were similar to those reported in spontaneous and experimentally induced hepatomas. RNA and nitrogen content did not differ appreciably from that of the controls, but the DNA content was 200% higher. This increased DNA content may be a reflection of changes in more than 1 cell population. Continued ability of megalohepatocytes to synthesize DNA would consistently result in the production of polyploid cells and an increase in DNA. Although there is some evidence that megalohepatocytes are instrumental in producing hepatomas, other findings are indicative of senility. The latter view was supported by the finding that the hepatocyte population decreased without appreciable regeneration, followed by liver failure.

70-2309 DEPENDENCE OF TUMOR FORMATION IN FROGS ON ABNORMAL NUCLEOLAR FUNCTION. Duryee, W. R., Pp. 82-100 in Biology of Amphibian Tumors, Mizell, M. (Ed.). Springer-Verlag, New York, 1969, 484 pp. (Recent Results Cancer Res., Special Suppl.).

Renal and pulmonary tumors developing in leopard frogs (*Rana pipiens*) maintained at 16° C. and admin. a 0.5 ml soln. of lead acetate or lead nitrate (0.03-0.05 M; p.o., weekly for 2-10 mo.) were examined in stained slides, tissue cultures and time-lapse cinephotography. After a 307-day latent period, the degree of abnormality (lymphocyte infiltration tubule hyperplasia, emboli) increased with time and duration of exposure. The primary target in the cell was the nucleolar organizer. All tumors exhibited marked hypersecretion of mucus from the outer columnar cells. Renal cells secreted mucins from rhythmically bursting surface vacuoles, this phenomenon being related to increased invasiveness of the cells. Rates of nucleolar RNA extrusion (halo formation) could be increased from av. times of 20-25 min./burst to 4 or 5 min. by increasing heat by 2.5° C; cooling markedly slowed nucleolar function. Actinomycin D blockage of nucleolar organizer DNA activity was always followed by cell shrinkage or 'negative growth'. Puromycin blockage of cytoplasmic protein synthesis also produced cell shrinkage. It is concluded that the nucleolar organizers are the genetic pacemakers for cell growth.

70-2310 NICKEL CARBONYL INHIBITION OF INDUCTION OF AMINOPYRINE DEMETHYLASE ACTIVITY IN LIVER AND LUNG. (E.) Sunderman, F. W., Jr. (U. Connecticut Sch. Med., Hartford) and K. C. Leibman. Cancer Res. 30(6):1645-1650, 1970.

Admin. of an LD₅₀ of nickel carbonyl by inhalation (0.20 mg Ni/liter air/15 min.) or i.v. inj. (2.2 mg Ni/100 g body wt.) inhibited aminopyrine demethylase activity in the livers of male Sprague-Dawley rats (90-100 g). The temporal sequence was different in otherwise untreated and phenobarbital-treated (7.5 mg/100 g body wt., i.p.) animals. Nickel carbonyl also inhibited aminopyrine demethylase activity induced in the rat lung by 10 mg/100 g body wt. of phenothiazine p.o.

70-2311 MOLECULAR BIOLOGICAL STUDIES OF ARSENIC-INDUCED CARCINOGENESIS. (Ger.) Jung, E. G. (U. Heidelberg Derm. Clin., Germany) and B. Trachsel. Arch. Klin. Exp. Derm. 237(3): 819-826, 1970.

When human epidermal cells derived from 7 normal men (age 20-30 yr.) were incubated for 1 hour with inorganically-bound arsenic (Na₂HAsO₄) or exposed to irradiation from a xenon lamp, with both treatments followed by 4-hour incubation with ³H-methylthymidine, the mitotic index was reduced significantly and to about the same degree. In cells receiving both treatments prior to labeling, the mitotic index was further reduced, confirming a cumulative effect. Arsenic-induced inhibition of the dark repair enzymatic mechanism was also demonstrable; no significant differences in this latter respect were found between the effects of 1 or 4 hours of incubation with the arsenic compound, or between the effects of conc. of 10⁻⁵ or 10⁻⁶ M.

70-2312 TOXICOLOGICAL STUDIES ON BERYLLIUM OXIDES AND BERYLLIUM-CONTAINING EXHAUST PRODUCTS. (E.) Spencer, H. C. (Dow Chem. Co., Midland, Mich.), R. H. Hook, J. A. Blumenshine, S. B. McCollister, S. E. Sadek and J. C. Jones. Aerospace Med. Res. Labs. AMRL-TR-68-148:1-236, 1968.

Biological activities (chronic pulmonary toxicities, translocation from the lungs to other tissues and effects on serum proteins) of beryllium oxides (BeO) and beryllium-containing exhaust products from motors fired by high-energy rocket propellants, were studied in rats, hamsters and rabbits. BeO samples calcined at 500° C for 10 hours showed marked biological activity; intratracheal inj. of these samples sometimes induced adenocarcinomas of the lung in rats observed for about 1 yr. The highest dose of the 500° C samples also caused a significant increase in serum γ-globulin levels in rats (but not in rabbits or hamsters).

veral beryllium-containing exhaust products showed similar biological activities. BeO samples calcined at 1100° C showed less biological activity than the 500° C samples; samples calcined at 1600° C showed minimal activity (resembling the effects of relatively "inert" dusts), as did a number of the exhaust samples. The BeO samples calcined at high temperatures caused no significant change in serum protein electrophoretic patterns in rats, rabbits or hamsters. Biologically active exhaust products were highly heterogeneous, containing large quantities of water-soluble beryllium. Biological activities of the samples tested decreased as the surface area decreased, and as the av. crystallite size, crystallinity, refractive index and density increased.

2313 BETEL-NUT-ASSOCIATED CANCER: REPORT OF CASE. (E.) Fendell, L. D. and J. Smith (377 USAF Dispensary, APO San Francisco, Calif.). J. Oral Surg. 28(6):455-456, 1970.

ions of the buccal mucosa, resembling a papilloma (later identified as a squamous carcinoma) and hyperkeratosis, were found in a 79-yr.-old Vietnamese woman with a long-term history of chewing betel nuts. The possible carcinogenic properties of the betel nut, either alone or in conjunction with lime and tobacco, are suggested.

2314 STUDIES ON CARCINOGENIC PROPERTIES OF BRACKEN, *Pteridium aquilinum*. (E.) Ono, I. (Gifu U. Sch. Med., Gifu-City, Japan), Shibuya, K. Fushimi and M. Haga. J. Nat. Cancer Inst. 45(1):179-188, 1970.

Male and female, 1-mo.-old ACI rats were fed either unprocessed bracken (UB; *Pteridium aquilinum*; in pellets x 4 mo.), processed bracken (PB) treated with boiling water (as above) or extracted water of bracken (in the drinking water x 18-27 days). Tumors (adenomas, adenocarcinomas and sarcomas) of the ileal region, or some of the cecum, developed in all rats treated with UB that survived more than 7 mo. With PB, the latent period was increased and the frequency of intestinal tumors (no sarcomas) was decreased; however, more urinary bladder tumors developed than in controls. The extracted water of bracken induced no tumors. It is suggested that treatment with boiling water removes the carcinogen from bracken, and that long-term ingestion of small amounts of bracken carcinogen results in a high frequency of intestinal and urinary bladder tumors.

2315 FEEDING STUDIES ON SODIUM CYCLAMATE, SACCHARIN AND SUCROSE FOR CARCINOGENIC AND TUMOUR-PROMOTING ACTIVITY. (E.) Roe, F. J. Chester Beatty Res. Inst. Cancer Res., London, L. S. Levy and R. L. Carter. Food Cosmet. Toxic. 8(2):135-145, 1970.

Female Swiss mice were fed a standard diet containing sucrose (10%), sodium cyclamate (5%) or saccharin (5%) for 18 mo. following pretreatment with polyethylene glycol (PEG; 0.2 ml, by gastric intubation) or 3,4-benzpyrene (BP; 50 µg, in PEG). Although BP increased the frequency of tumors of the forestomach epithelium, further increases due to the sweetening agents, as cocarcinogens, were not observed. None of the sweeteners induced g.i. tumors or affected the occurrence of tumors of other organs, when admin. alone. No urinary bladder tumors were detected by macroscopic examination in any of the mice. It is concluded that the sweetening agents had no carcinogenic or cocarcinogenic activity under these experimental conditions.

70-2316 Δ⁸- AND Δ⁹-TETRAHYDROCANNABINOL: EFFECTS ON CULTURED HUMAN LEUCOCYTES. (E.) Neu, R. L. (State U. New York Upstate Med. Ctr., Syracuse), H. O. Powers, S. King and L. I. Gardner. J. Clin. Pharmacol. 10(4):228-230, 1970.

Human WBC cultures inoc. with Δ⁸-tetrahydrocannabinol (Δ⁸-THC in absolute ethyl alcohol solvent; 30-45 µg/ml medium) demonstrated a drastically decreased mitotic index for all Δ⁸-THC conc., with the lowest mitotic index occurring for the highest conc. No more than 5% of the metaphases in control or experimental cultures had gaps and breaks, and no additional structural changes were observed. Similar results were found in preliminary studies with Δ⁹-THC.

70-2317 LUNG HYDROXYPROLINE LEVELS IN MICE EXPOSED TO CIGARETTE SMOKE. (E.) Rosenkrantz, H. (Mason Res. Inst., Worcester, Mass.), H. J. Esber and R. Sprague. Life Sci. 8, Pt. 1(11):571-576, 1969.

Male and female Swiss albino mice (24-35 g) were exposed to whole smoke (total time of 250-950 min. over a period of 5-19 days, resp.). Examination of organs included hydroxyproline (HP), collagen and total nitrogen determinations on the lungs and livers. Exposure to whole smoke reduced body wt. by 5-12%. Results did not vary significantly with sex or time, but a dose-dependent increase (from 27% to 67% for 250 and 905 min. exposure, resp.) was observed in HP levels of the lungs. It is concluded that increased HP indicates that synthesis of free amino acid has occurred which leads to collagen formation; HP can, thus, be used as a parameter to estimate tissue damage by tobacco smoke.

70-2318 ON THE CARCINOGENIC FACTORS OF TOBACCO LEAF POWDER. I. INHALATION OF TOBACCO LEAF POWDER. (Jap.) Hamazaki, Y. (Okayama U., Japan) and T. Murao. J. Karyopath. 12(3):163-178, 1969.

The results of experiments in which Strong A and Swiss mice inhaled tobacco leaf powder for 30 mo. (dose unspecified) indicates that water-soluble substances in tobacco are strong carcinogens. Thus, inhalation of fine tobacco powder, particularly by chewing tobacco and snuff users, may play a role in the development of human lung cancer. Lung cancer developed in 12 (16%) of the experimental mice, leukemia in 11 (14%), and malignant liver tumors in 3. Benign tumors included 5 hepatic adenomas and 6 adenomas of other sites. Of the 12 mice with lung cancer, 6 had alveolar cell carcinomas, 3 had squamous cell carcinomas, and 3 had malignant adenomas. Alveolar cell carcinomas tended to be undifferentiated. In 3 cases they metastasized into the pleura and mediastinum. Malignant tumors also developed in some of the controls, inhaling tobacco leaf powder which had been washed in water until the nicotine reaction disappeared. These included 2 cases of leukemia and 1 malignant pulmonary adenoma. Since leukemia in experimental mice did not differ from spontaneous leukemia, it is concluded that tobacco leaf components may activate leukemia latent in normal mice. No strain differences were noted in the incidence or location of tumors.

70-2319 PROPOSED CLASSIFICATION FOR BRONCHIAL EPITHELIAL CELL ABNORMALITIES IN THE CATEGORY OF DYSKARYOSIS. (E.) Fullmer, C. D. (Holy Cross Hosp., Salt Lake City, Utah), J. G. Short, A. Allen and K. Walker. Acta Cytol. (Balt.) 13(8):459-471, 1969.

Data from a cytological study of all sputum and bronchial aspiration specimens collected since 1954 at Holy Cross Hospital, Salt Lake City, were used to form a table of classification of all types of bronchial epithelial abnormalities in an attempt to determine malignancies or pre-malignant conditions. In 100 pts. with pulmonary symptoms, including men (ages 39-81 yr.) with long histories of heavy smoking, dyskaryotic changes were attributed to a variety of causes: acute and chronic viral infections, post-irradiation changes, pneumoconiosis, bacterial and mycotic infection, fibrosis of the lungs and other lesions, radiomimetic compounds (busulfan or cyclophosphamide). The various levels of dyskaryosis were presented in a formal classification scheme. It is suggested that results of such classification of bronchial epithelium are similar to those in testing for carcinoma of the cervix.

70-2320 RELATIONSHIP BETWEEN PNEUMOCONIOSIS AND LUNG CANCER. (Jap.) Sano, T. Rodo Kagaku (J. Sci. Labour (Tokyo)) 45(7): 383-396, 1969.

Relationship between various forms of pneumoconiosis and development of lung cancer is discussed with emphasis on the frequency of

asbestosis (with hyperplasia and squamous cell metaplasia) and its carcinogenic effects on lung tissues. Study of cases of silicosis and lung cancer showed 3/20 and 7/20 with Class I and II scar carcinomas, resp. The association of other pneumoconiosis forms (alumina lung, pyrophyllite pneumoconiosis, welder's lung and activated carbon lung) with epithelial changes is also discussed.

70-2321 LUNG CANCER OCCURRING WITH PNEUMOCONIOSIS AND HISTOLOGICAL STUDY OF THE BRONCHIAL EPITHELIUM. (Jap.) Nishimura, M. (Kinkishuo-Byoin Nat. Sanatorium, Japan) and Y. Sera. Iryo 23(2):194-203, 1969.

Study of the association of lung cancer and pneumoconiosis showed asbestosis to be significantly related to malignant tumors. In an autopsy study, 7 cases of pneumoconiosis were found among pts. with lung carcinoma, including 3 cases of silicosis, 2 of asbestosis, and 1 each of pyrophyllite pneumoconiosis and welder's lung. Squamous cell metaplasia and basal cell hyperplasia were found in 19.3% and 63.0%, resp., of pts. with associated asbestosis and cancer.

70-2322 TUMOR INDUCTION IN Nicotiana glauca x N. langsdorffii SEEDLINGS BY A TOBACCO SMOKE CONDENSATE FRACTION. (E.) Andersen, R. A. (US Dept. Agric. Crops Res. Div., Lexington, Ky.) and J. A. Sowers. Fed. Proc. 29(2):808, 1970.

70-2323 ENHANCEMENT OF RECOVERY FROM CILIASTASIS AFTER CIGARETTE SMOKE EXPOSURE BY ALUPENTR^R (METAPROTERENOL) AEROSOL TO RABBIT TRACHEA IN-VITRO. (E.) Bleiberg, M. J. (Woodard Res. Corp., Herndon, Va.). Fed. Proc. 29(2):550, 1970.

70-2324 BILIARY EXCRETION OF BENZOPYRENE IN THE RAT. ROLE OF MICROSOMAL ENZYMES. (E.) Levine, W. G. (Albert Einstein Coll. Med., Bronx, N. Y.). Fed. Proc. 29(2):543, 1970.

70-2325 ALTERATIONS IN LIVER NUCLEOPROTEIN AFTER ADMINISTRATION OF 3-METHYL-CHOLANTHRENE (3MC). (E.) Bresnick, E. (Baylor Coll. Med., Houston, Tex.). Fed. Proc. 29(2): 737, 1970.

70-2326 DIFFERENCES IN THE HEPATIC CYTOCHROME P-420 OBTAINED FROM NORMAL AND 3-METHYL-CHOLANTHRENE (MC) TREATED RATS. (E.) Shoeman, D. W. (U. Minnesota, Minneapolis), F. Vane and G. J. Mannering. Fed. Proc. 29(2):738, 1970.

-2327 ABSORPTION OF INTRAGASTRICALLY
ADMINISTERED 7,12-DIMETHYLBENZANTHRA-
NE. (E.) Janss, D. H. (U. Tennessee Med.
its, Memphis) and R. C. Moon. Fed. Proc.
(2):817, 1970.

-2328 STOMACH LESIONS IN MICE MAINTAINED ON
A DIET SUPPLEMENTED WITH CRUDE CORN
.. (E.) Szepeswol, J. (U. Puerto Rico Sch.
l., San Juan). Fed. Proc. 29(2):818, 1970.

70-2329 EFFECTS OF ADMINISTRATION OF POLY-
CYCLIC HYDROCARBON CARCINOGENS DURING
PREGNANCY ON THE PROGENY. (E.) Bulay, O. M. (U.
Minnesota Med. Sch., Minneapolis) and L. W.
Wattenberg. Fed. Proc. 29(2):818, 1970.

70-2330 PROMOTION OF AFLATOXIN-INDUCED HEPA-
TOMA GROWTH BY CYCLOPROPENOID FATTY
ACIDS. (E.) Lee, D. J. (Oregon State U.,
Corvallis), J. H. Wales, R. O. Sinnhuber and
J. N. Roehm. Fed. Proc. 29(2):568, 1970.

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2533,2535,2536,2538,2539,2540,2541,2542,2543,2544,2545,2552,2560,2561,2580,
2629,2642,2652

70-2331 AGE DEPENDENCE OF IMMUNOLOGICALLY INDUCED CENTRAL NERVOUS SYSTEM DISEASE IN C58 MICE. (E.) Murphy, W. H. (U. Michigan Sch. Med., Ann Arbor), M. R. Tam, R. L. Lanzi, M. R. Abell and C. Kauffman. Cancer Res. 30(6): 1612-1622, 1970.

About 60% of old (10-14 mo.) C58/wm mice, immunized with syngenic I_b cells, developed an age-dependent disease of the central nervous system (CNS) characterized by monocytic inflammation and infiltration, primarily confined to the grey matter of the spinal cord; some demyelination and destruction of neurons in the cord; and paralysis or death. The CNS disease could be induced in old, but not in young (2-6-mo.) C58/wm mice by i.p. inj. of lymphoid cells or serum from animals with CNS disease or by i.p. inj. of peritoneal cells from normal young C58/wm mice which had been incubated with serum from mice with CNS disease. BALB/wm mice did not develop the CNS disease. No neuropathogenic virus was detected in CNS tissues or in line I_b cell suspensions. Unsuccessful attempts were made to induce CNS disease in young and old C58/wm mice by immunization with a leukemogenic virus (T/S) derived from line I_b cells and by immunization with virus-rich spleen cells from C58 mice with spontaneous leukemia. All cell fractions (nuclei, mitochondria, microsomes, membranes) of line I_b, obtained by differential centrifugation and density gradient fractionation, induced CNS disease in old C58 mice. It is suggested that the CNS disease induced in C58/wm mice might result from a serum-mediated immunological response directed against θ -type iso-antigens presumed to be present in leukemic cells and CNS tissue. It is postulated that as mice age there is a low-grade, but progressive, antibody response to altered CNS antigens.

70-2332 ULTRASTRUCTURAL ASPECTS OF ANTIBODY PLAQUE-FORMING CELLS FROM CLINICALLY NORMAL AND OVERTLY AUTOIMMUNE NZB MICE. (E.) Siegel, B. V. (U. Oregon Med. Sch., Portland), R. E. Brooks and J. I. Morton. Blood 35(3): 386-393, 1970.

Electron microscopic study was made of antibody plaque-forming cells from the spleens of 6-8-week-old and Coombs¹-positive, 9-11-mo.-old NZB mice and 6-8-week-old and 10-14-mo.-old BALB/c mice, inj. i.p. with 1.5×10^9 saline-washed sheep RBC. Older BALB/c mice had somewhat higher conc. of antibody-producing cells/mg spleen than the young animals of this strain. Spleens of young NZB mice had considerably more plaque-forming cells than either BALB/c group, while plaque formation by old NZB mice was markedly decreased. The ultrastructure of antibody-producing cells from immunologically hyperactive young NZB mice was similar to that of cells from overtly autoimmune old NZB mice with

depressed immune responsiveness, but in the older animals there was more extensive dilatation of the endoplasmic reticulum and some of these cells exhibited increased fragility. In contrast to murine leukemia Type C particles found in the organs of NZB mice, intracisternal virus-like particles lacked an electron-dense nucleoid and did not bud from the cytoplasmic membranes. Since these virus-like particles were found in antibody-producing cells of young and old BALB/c mice, as well as in those of the NZB strain, it is unlikely that they are responsible for the development of autoimmune disease or malignancy.

70-2333 FOCUS FORMATION BY A MURINE SARCOMA-LEUKEMIA VIRUS COMPLEX. I. THEORETICAL ANALYSIS. (E.) Hahn, G. M. (Stanford U. Sch. Med., Calif.), A. Declève, M. Lieberman and H. S. Kaplan. J. Virol. 5(4):432-436, 1970.

Quantitative analysis was made of interactions occurring between leukemia virus, defective sarcoma particles and competent hybrid particles in the transformation of cell cultures by a murine sarcoma-leukemia virus complex. By means of Poisson statistics, equations are derived which make it possible to estimate the conc. of the various virus types and to assay leukemia virus preparations *in vitro*. Analysis is based on the statistical distribution of virions in the culture cells and the assumption that all virions have equal probability of infecting a cell and that transformation of any one cell will lead to focus formation.

70-2334 FOCUS FORMATION BY A MURINE SARCOMA-LEUKEMIA VIRUS COMPLEX. II. QUANTITATIVE ASPECTS OF THE INTERACTION BETWEEN RADIATION LEUKEMIA VIRUS AND ITS MURINE SARCOMA VIRUS PSEUDOTYPE IN STRAIN C57BL MOUSE EMBRYO CELLS. (E.) Declève, A. (Ctr. Study Nuclear Energy, Mol-Donk, Belgium), M. Lieberman, G. M. Hahn and H. S. Kaplan. J. Virol. 5(4):437-445, 1970.

By using equations developed in the preceding paper, a quantitative study was made of interactions between radiation leukemia virus (RadLV), its murine sarcoma virus pseudotype and host cells of C57BL/Ka mouse embryo fibroblasts. Interference exerted by exogenous RadLV against murine sarcoma virus pseudotype was eliminated in the helper assay by adding RadLV to the cultures 1 hour after infection with murine sarcoma virus. This procedure also resulted in a predictable level of focus-formation and was rapid enough so that host cells were less likely to be damaged. It was found that the murine sarcoma virus pseudotype consists of defective sarcoma particles, endogenous RadLV, and competent particles which are probably aggregates of the other two types. The ratio of leukemia to defective particles (10^4 :1) is higher than

ratios observed with other pseudotypes. These results, however, were based on the assumption that RadLV and competent hybrids are equally efficient in infecting host cells. It is concluded that the assumptions on which this theory is based approximate actual biological conditions.

70-2335 IMMUNE VIROLYSIS: EFFECT OF ANTIBODY AND COMPLEMENT ON C-TYPE RNA VIRUS.

(E.) Oroszlan, S. (Flow Labs. Inc., Rockville, Md.) and R. V. Gilden. Science 168(3938): 1478-1480, 1970.

When the AKR strain of mouse leukemia virus was lysed in the presence of envelope antibody and complement (C'), viral RNA became susceptible to RNase digestion, and the internal group-specific antigen was released. These data support the concept of virolysis by antibody and C' because intraviral components are released by their combined action. Since antibody to an "internal" virion antigen was nonlytic, the specificity of the antiserum and the true internal localization of the group-specific antigen were confirmed. These observations provide a basis for a relatively rapid method to detect envelope antibody to C-type viruses and (using inhibition methods) the corresponding antigen.

70-2336 Fv-2: IDENTIFICATION AND LOCATION OF A SECOND GENE GOVERNING THE SPLEEN

FOCUS RESPONSE TO FRIEND LEUKEMIA VIRUS IN MICE. (E.) Lilly, F. (Albert Einstein Coll. Med., Bronx, N. Y.). J. Nat. Cancer Res. 45(1):163-169, 1970.

The F-S strain and F-B strain (a BALB/c-adapted variant) of Friend leukemia virus (FLV) were used in studies that identified a second major gene which distinguishes the varied spleen-focus response to virus of the DBA/2J and C57BL mouse strains. DBA/2 and C57BL mice were susceptible and resistant to both virus strains, resp. A new gene, Fv-2, segregating independently of the previously identified gene, Fv-1, was identified in progeny testing of (C57BL x DBA/2J) x DBA/2J backcross females. Little influence by the Fv-1 locus (with spleen-focus response to F-S virus) was exerted on the expression of the Fv-2 phenotype (with spleen-focus response to F-B virus). It is suggested that a helper virus was required in spleen-focus formation by FLV.

70-2337 INTERFERENCE OF COCAL VIRUS WITH FRIEND LEUKEMIA VIRUS-INDUCED SPLENO-

MEGALY IN DBA/2J MICE. (E.) Stim, T. B. (Yale Sch. Med., New Haven, Conn.). Proc. Soc. Exp. Biol. Med. 134(2):413-420, 1970.

Male DBA/2J mice were inoc. i.p. with coval arbovirus (CV) from 5 days before to 5 days after inoc. with Friend leukemia virus (FLV). Development of splenomegaly was observed until

10-14 days after FLV admin. Rate of splenomegaly development was directly related to amount of FLV admin. (palpable spleens were noted 7-10 days and 15-56 days after inoc. for the high and low doses, resp.). Admin. of CV interfered with FLV induction of splenomegaly, as measured by spleen wt. CV-treated mice (62-87%) had spleen wt. less than that of FLV-treated mice. Greatest reduction of spleen enlargement was seen for mice treated with CV 36-48 hours before FLV was admin. Inactivation of CV with UV treatment resulted in a decrease of the antileukemic effect; inoc. of CV delayed deaths due to leukemia, but did not provide permanent protection. The possible use of CV as a therapeutic agent, alone or in conjunction with others, in cases of human leukemia is suggested.

70-2338 IMMUNOCOMPETENT CELL FUNCTIONS IN MICE INFECTED WITH FRIEND LEUKEMIA VIRUS.

(E.) Bennett, M. (Roswell Park Mem. Inst., Buffalo, N. Y.) and R. A. Steeves. J. Nat. Cancer Inst. 44(5):1107-1119, 1970.

Results of experiments on immunocompetent cell functions in mice indicate that Friend leukemia virus (FLV) directly and selectively depresses the bone marrow component of the humoral antibody response. Antigen-sensitive units of lymph nodes responsive to sheep RBC antigens and leading to the formation of hemolytic plaque-forming cells were suppressed by infection with the Axelrad strain of FLV, which induced spleen focus formation and polycythemia in susceptible mice. Marrow precursors of plaque-forming cells were markedly suppressed by FLV infection. Spleen focus formation was enhanced in susceptible mice by cortisol, which also suppresses marrow precursors of plaque-forming cells. Thus, interaction between FLV and immunocompetent cells analogous to these precursors was not required for viral induction of erythropoiesis. Preliminary treatment with cortisol did not make C57BL/10 mice, which are genetically refractory to most strains of FLV, susceptible to spleen focus formation. Therefore, the cellular basis for this genetic refractoriness to FLV does not reside in immunocompetent precursors, but probably resides in erythropoietic "target" cells. FLV infection did not impair graft-versus-host reactions in irradiated mice infused i.v. with viable spleen cells from allogeneic donor mice. These reactions were noted irrespective of whether donor or host mice were infected with FLV.

70-2339 INHERITANCE OF SUSCEPTIBILITY TO FRIEND MOUSE LEUKEMIA VIRUS. V. INTRODUCTION OF A GENE RESPONSIBLE FOR SUSCEPTIBILITY IN THE GENETIC COMPLEMENT OF RESISTANT MICE. (E.) Odaka, T. (U. Tokyo Inst. Med. Sci., Takanawa). J. Virol. 3(6):543-548, 1969.

By means of backcrossing and brother-sister mating in the generation 8, a gene (Fv^S) responsible for the susceptibility of mice to Friend leukemia virus (FLV) was introduced from the susceptible DDD strain into the genetic complement of resistant C57BL mice. Male DDD mice were mated with female C57BL/6 mice and heterozygotes for Fv^S were selected by the progeny test at each generation. The effect of this gene was not diluted out during successive backcrosses, and the phenotypes and genotypes of the progeny obtained agree well with the hypothesis that a single gene or group of closely linked genes controls the susceptibility of mice to FLV. However, this does not exclude the possibility that several minor genes also influence development of Friend leukemia. Mice homozygous for Fv^S were obtained by brother-sister mating. These homozygotes and their progeny produced by incross could be assumed congenic with C57BL/6 mice except for susceptibility to FLV.

70-2340 INHERITANCE OF SUSCEPTIBILITY TO FRIEND MOUSE LEUKEMIA VIRUS. VI. RECIPROCAL ALTERATION OF INNATE RESISTANCE OR SUSCEPTIBILITY BY BONE MARROW TRANSPLANTATION BETWEEN CONGENIC STRAINS. (E.) Odaka, T. (Inst. Med. Sci., Takanawa, Tokyo) and M. Matsukura. *J. Virol.* 4(6):837-843, 1969.

A study of the effects of bone-marrow transplantation in 2 newly established mouse strains which are congenic with the DDD and C57BL strains suggest that the effect of the gene locus (Fv) responsible for sensitivity or resistance to Friend leukemia virus (FLV) is expressed in bone-marrow derived cells and that they play a major role in the development of splenomegaly which occurs with FLV infection. Congenic strains of mice have the same major histocompatibility gene but have different Fv loci. Splenomegaly did not develop in mice with the Fv^r/Fv^r genotype (DDD- Fv^r , C57BL/6) while mice with the Fv^S/Fv^S genotype (DDD, C57BL/6- Fv^S) developed splenomegaly even when they were inj. i.p. with 10^{-3} - 10^{-5} -fold the dose given resistant strains. Mice of each strain were exposed to 700-900 r of whole-body irradiation, inoc. with bone marrow cells from either syngenic or congenic mice, and challenged later with FLV. Leukemia did not develop when Fv^S/Fv^S mice were given bone marrow transplants taken from Fv^r/Fv^r mice, but Fv^r/Fv^r mice developed marked splenomegaly after receiving Fv^S/Fv^S bone marrow cells. High titers of infectious virus were found in the enlarged spleens of C57BL/6 mice which are ordinarily resistant to FLV infection. These changes in the response of mice to FLV infection appear to be caused by repopulation of destroyed tissues by the transplanted bone marrow cells.

70-2341 ANTIGENIC VARIANT (WFT-2N) OF A TRANSPLANTABLE RAT TUMOR INDUCED BY FRIEND VIRUS. (E.) Kobayashi, H. (Hokkaido U. Sch.

Med. Cancer Inst., Sapporo, Japan), T. Shirai, T. Takeichi, M. Hosokawa, H. Saito, F. Sento and T. Kodama. *Rev. Europ. Etud. Clin. Biol.* 15(4): 426-428, 1970.

Transplantable rat tumors induced by Friend virus (RFT), that do not usually grow in isologous normal adult rats, grew well in Friend virus-tolerant rats inj. with Friend virus at birth or in rats in depressed immunological states. A variant line (WFT-2N) was obtained from WFT-2 which grew well in normal adult rats. The antigenic behavior of WFT-2N cells was compared with 3 other lines. Results from both immunocytotoxic and membrane fluorescence tests were inversely correlated with the growth of the Friend tumors, thus either no membrane antigens existed or they were in very low conc. in the WFT-2N cells. WFT-2N does have transplantation antigen as shown by an *in vivo* transplantation experiment. With WFT-2N the transplantation antigen is less sensitive and can be detected less readily in the *in vitro* than in the *in vivo* system.

70-2342 REPLICATION OF FRIEND LEUKEMIA VIRUS IN THE CELLS OF TRANSPLANTED SARCOMA 180. (Rus.) Merekalova, Z. I. (Inst. Exp. Clin. Oncol., Moscow). *Vop. Onkol.* 16(2):66-68, 1970.

Healthy BALB/c mice were inj. with Friend leukemia virus (FLV) and s.c. with cells of Sarcoma 180. These mice developed leukemia and large s.c. tumors simultaneously, as did mice in the next 5 generations. No symptoms of leukemia were found in mice inj. with Sarcoma 180 from generations 6-14 of these mice, but leukemia was induced in mice by i.p. inj. of cell-free spleen extracts from mice up to generation 14. FLV was detected *in vitro* in the first 5 passages of Sarcoma 180 cells after 2 generations in mice. It is suggested that cells from transplanted tumors carry low levels of leukemia-inducing viruses for a long time.

70-2343 EVIDENCE FOR TRANSFORMATION OF SPLEEN CELLS ON DAY AFTER INFECTION OF MICE WITH FRIEND LEUKEMIA VIRUS. AUTONOMOUS GROWTH POTENTIAL AND EXPRESSION OF HYBRID-RESISTANCE GENES. (E.) Rossi, G. B. (Superior Inst. Sanit., Rome), G. Cudkowicz and C. Friend. *J. Exp. Med.* 13(4):765-781, 1970.

Spleen colony or ^{125}I -2'-deoxyuridine- ^{59}Fe -uptake methods were used to assay proliferation and erythroid differentiation in transplanted DBA/2 bone marrow cells, in syngenic and allogenic (H-2 compatible), X-irradiated and nonirradiated (BALB/c x DAB/2) F_1 hybrid (CDF $_1$) mice, 5 days after transplantation of DBA/2 bone marrow cells and cells of a leukemia induced by Friend leukemia virus (FLV). As compared to growth patterns in syngenic and allogenic hosts, DBA/2J bone marrow grafts grew poorly in X-irradiated CDF $_1$ J

hybrids. These grafts grew quite well in X-irradiated CDF₁J hybrids bred from male CBA/2J sublines (Ha, Cr and Cum). Leukemic cells of DBA/2J origin grew poorly in all CDF₁ hybrid strains studied, irrespective of the DBA/2 parental subline or the type of irradiation. In CDF₁ Ha hybrids, DBA/2J hematopoietic cells showed a compromised growth pattern, which began within 6 hours of *in vivo* infection with FLV and lasted for 8 days. Results of experiments using grafts from DBA/2 sublines suggested that hybrid histocompatibility alleles were expressed to a greater extent in leukemic cells than in normal bone marrow cells.

70-2344 ELECTRON MICROSCOPIC STUDIES ON RAT TUMOR CELLS INFECTED WITH MOUSE FRIEND LEUKEMIA VIRUS. (Jap.) Kodama, T. (Hokkaido U. Sch. Med. Cancer Inst., Sapporo, Japan), H. Saito and H. Kobayashi. Virus (Osaka) 19(1):14-22, 1969.

Mice were inoc. with Friend leukemia virus (FLV; $10^{4.5}-10^{5.5}$ ID₅₀/ml) and, from 10-20 days later, assorted rat tumors were implanted into these animals. Tumors included spontaneous undifferentiated sarcomas, 4-nitroquinoline 1-oxide-induced undifferentiated lung carcinomas and azo dye-induced hepatomas. Electron microscopy showed virus development in the cell membranes of the tumor cells in all cases. Ferritin antibodies were observed in developing virus particles of all tumor cells. In a comparison with control tumor cells, it was noted that FLV did not show any effect on the infected cells in terms of cell development.

0-2345 TRANSFORMATION OF CANCER CELLS. (Jap.) Sendo, F. (Hokkaido U. Cancer Inst., Sapporo, Japan) and H. Kobayashi. Saishin Igaku 5(5):1012-1017, 1970.

Rats were inoc. with 3 different types of malignant cells after infection with Friend leukemia virus (FLV). No animals died which had received implants of the WST-5 spindle cell sarcoma and the DLT undifferentiated lung carcinoma following the FLV treatment, as opposed to 3/14 rats with Takeda sarcomas and 6/12 mice with AH-109A ascitic hepatoma. All 15 rats inj. with FLV-infected Takeda sarcoma cells survived. However, all 29 rats "protected" with FLV and receiving s.c. implantation of the spindle cell sarcoma and the undifferentiated lung carcinoma died with tumors. When 3-methylcholanthrene (5 mg/kg)-induced tumors were implanted i.p. into rats inoc. with FLV, tumors developed in 10 days, then regressed, while tumors continued to grow in non-inoc. rats.

-2346 EFFECT OF EXOGENOUS AND ENDOGENOUS INTERFERON ON THE COURSE OF LEUKEMIA INDUCED IN MICE WITH FRIEND VIRUS. (Rus.)

Sabashvili, M. K. (Cent. Inst. Hemat. Blood Transfus., Moscow) and N. M. Furer. Antibiotiki 15(1):52-55, 1970.

Leukemia was induced in BALB/c mice (18-20 g) by i.p. inj. of a cell-free extract from the spleens of mice with Friend leukemia. The development of leukemia, as measured by the wt. of the spleens, was significantly inhibited in mice inj. i.p. with exogenous interferon 3 hours before inj. of leukemia virus and every day thereafter. This interferon was obtained by inoc. of mouse cell line L with Newcastle disease virus. No effect was noted when interferon was inj. 24 hours after admin. of leukemia virus and every day thereafter. Development of leukemia was also inhibited by inj. of prodigiosan (Pr; 20 µg, i.p.) 8 hours before inj. of Friend leukemia virus (FLV) and every 3 days thereafter. Pr is a polysaccharide isolated from *Serratia marcescens*, previously noted as a stimulator of endogenous interferon production. Combined admin. of exogenous interferon and Pr inhibited development of leukemia more than admin. of either alone.

70-2347 AUTOIMMUNE DISEASE IN NEW ZEALAND BLACK MICE INFECTED WITH RAUSCHER LEUKEMIA VIRUS. (E.) Siegel, B. V. (U. Oregon Med. Sch., Portland) and J. I. Morton. J. Nat. Cancer Inst. 45(1):189-193, 1970.

Young adult NZB mice were inoc. with Rauscher leukemia virus (RLV; i.p.) and splenomegaly and anemia were seen at autoantibody assay in 26-27 days, in conjunction with a negative Coombs' reaction which indicated no acceleration of the autoimmune process. Inoc. of RLV to 6-week-old NZB mice showed a delayed appearance of a positive Coombs' test; with BALB/c mice, tests remained negative throughout the experiment. Coombs'-positive, 11-13-mo.-old NZB mice inoc. with RLV showed leukemogenesis unassociated with a reversal of the positive Coombs' reaction. It is concluded that RLV effects on autoantibody formation are similar to those for formation of antibodies to foreign antigens. A competition between virus and antigen may be the cause of such observed immunosuppression.

70-2348 DETECTION OF GROUP-SPECIFIC VIRUS ANTIGEN IN NORMAL MICE OF HIGH- AND LOW-LEUKEMIA STRAINS. (Rus.) Ilevleva, E. S. (N. F. Gamalei Inst. Epidemiol. Microbiol., Moscow), N. B. Engel'gardt and G. I. Abelev. Biull. Eksp. Biol. Med. 68(10):73-77, 1969.

Group-specific antigen (GSA) of mouse leukemia viruses was detected in the spleens of normal mice from high- and low-leukemia strains by precipitating rabbit serum to GSA. Antibodies (Ab) to GSA were found in the antiserum of 1/2 rabbits immunized with Rauscher leukemia virus (RLV; with Freund's adjuvant; inj. into the popliteal lymph

nodes of the hind paws); max. Ab titer was found by days 10 and 12 after reimmunization (1 mo. after initial inj., RLV diluted with Ringer soln. was inj. i.m. or s.c. as above); Ab were then detected until day 18 after reimmunization. Antiserum was not monospecific; it contained Ab to γ - and α_2 -globulins of mouse serum in traces, and an antigen, found in high conc. in spleen and plasma of mice with Rauscher and Friend leukemia, and, in traces, in sera of normal mice but not in other leukemias. Rabbit antiserum neutralized with mouse serum usually contained only precipitating Ab to GSA (1:1 or 1:1.5) and was used as monospecific anti-GSA serum in the agar precipitation reaction, while the spleen of mice with RLV was used as antigen (1:3). GSA was present in the spleen of mice (newborn, 10-14 days old, 1.5 mo. old) of strains AKR (high-leukemia strain), BALB/c, Af, CC57Br and CC57W (low-leukemia strains) or C57BL/6 and C57BL/He (leukemia-resistant), and was absent in strains C57BL/10Sn and B10D2; in the latter 2 strains of mice with 3-methylcholanthrene (MC)-induced sarcomas, GSA was found in high conc. in the tumor. GSA was also present in MC and Rous virus-induced sarcomas of mice and was absent in polyoma or Rous virus-induced sarcomas of rats. The widespread occurrence of GSA in different mouse strains and in mice of all ages indicates mouse tolerance toward this antigen, in contrast to rats which do not carry leukemia virus or have GSA under normal conditions; rats readily form Ab to GSA.

70-2349 HISTOPROLIFERATIVE EFFECT OF RAUSCHER LEUKEMIA VIRUS ON LYMPHATIC TISSUE: HISTOLOGICAL AND ULTRASTRUCTURAL STUDIES OF GERMINAL CENTERS AND THEIR RELATION TO LEUKEMOGENESIS. (E.) Hanna, M. G., Jr. (Oak Ridge Nat. Lab., Tenn.), A. K. Szakal and R. L. Tyndall. Cancer Res. 30(6):1748-1763, 1970.

Histological and ultrastructural changes were studied in the spleen, thymus and mesenteric lymph nodes from adult BALB/c mice 6 hours to 20 days after i.p. inj. of Rauscher leukemia virus (RLV). Enlargement of germinal centers, observed 24 hours after infection, is attributed to hyperplasia of parenchymal immunoblasts, and cellular disorganization in these centers corresponds to "dissociative growth" of germinal centers characteristic of immune responses. Cells morphologically indistinguishable from those originally observed proliferating in the centers were dispersed throughout the spleen red pulp between 4 to 7 days after inj. of RLV. Type C particles were observed in germinal centers in both the spleen and mesenteric lymph nodes 6-24 hours after inj. of RLV. These particles were usually found extracellularly between plasma membrane infoldings of reticular cells which constitute the stroma of the centers. Type C particles were seen budding from parenchymal immunoblasts of the germinal centers as early as 24 hours after inj. After 7 days, virus-replicating

immunoblasts were found in the spleen red pulp in close association with hematopoietic cells. The temporal sequence of these events suggests that the immunoblasts may provide a source of Type C virus to proliferating megakaryocytes and RBC precursors in the spleen red pulp because immunoblasts: (1) apparently lose their ability to mature with concomitant loss of normal cell function; (2) undergo morphological changes previously attributed to leukemic cells; (3) participate in replication of C-type virus; and (4) undergo phagocytosis and degradation in the Kupffer cells of the liver. Viropexis among these cells in the red pulp was observed 10-20 days after infection.

70-2350 COMPARATIVE STUDY OF THE PROPERTIES AND ACTIVITY OF TETRAHYDROFOLATE DEHYDROGENASE IN THE LIVER AND SPLEEN OF MICE WITH VIRAL LEUKEMIA. (Rus.) Sergeev, A. V. (Inst. Exp. Clin. Oncol., Moscow). Vop. Med. Khim. 14(6):606-611, 1968.

Relationships between activity and pH and between activity and aminopterin conc. were the same in tetrahydrofolate dehydrogenase (THFD) from the liver and spleen of normal mice and in THFD from mice infected with Moloney, Rauscher and Friend leukemia viruses. Experiments were performed on 3-mo.-old male and female BALB/c and C57BL mice given an i.p. inj. of spleen cells or spleen extract from mice with Moloney, Rauscher or Friend leukemia. All of these preparations had 2 pH optima, 1 in the acid and 1 in the alkaline region; were inhibited 50% by aminopterin in conc. of 1.15×10^{-8} - 1.3×10^{-8} M at pH 7.4; and reduced dihydrofolic, but not folic, acid. In acid medium, reduced nicotinamide adenine dinucleotide phosphate (NADPH) was 6-fold more active as a coenzyme than NADH. Aminopterin had a greater affinity for THFD at pH 5.5 than at pH 7.5, and inhibited THFD more in acid medium. The THFD activity in the spleens of mice with Friend, Rauscher and Moloney leukemia was 110-, 42- and 14.5-fold, resp., the THFD activity in the spleens of normal mice. This increase was due both to an increased spleen wt. and a 1.5-4.5-fold increase in the specific activity of the enzyme. In contrast, THFD activity was only 1.2-1.7-fold the normal value in the livers of mice with Rauscher leukemia and remained normal in mice with Friend leukemia. The livers of mice with Moloney leukemia were 3.4-fold heavier than normal mouse livers, but the specific activity of THFD was reduced. This is apparently due to an invasion of the liver by leukemia cells in which the specific activity of THFD is somewhat lower than in the liver.

70-2351 E ANTIGEN: A CELL-SURFACE ANTIGEN OF C57BL LEUKEMIAS. (E.) Aoki, T. (Sloan-Kettering Inst. Cancer Res., New York, N. Y.), B. Stuck, L. J. Old, U. Hämmerling and E. de Harven. Cancer Res. 30(1):244-251, 1970.

A new cell-surface antigen, called E antigen, which differs from the 4 previously identified antigens (G, FMR, TL, ML) associated with mouse leukemias, was found in C57BL/6 mice. Antisera were prepared in (C3H/An x 1)F₁ mice against a transplanted leukemia that had originally developed spontaneously in C57BL/6 mice. E antigen was detected after removal of cytotoxic antibodies to normal alloantigens by absorption *in vivo* in C57BL/6 mice. E antigen was found in other spontaneous leukemias of C57BL/6 origin and in the long-transplanted chemically induced leukemia, EL4. It was not found in any normal C57BL/6 tissues nor in leukemias induced in C57BL/6 mice with radiation or viruses (Gross, Moloney and Rauscher leukemias). No E antigen was found in 39 solid tumors and leukemias originating in other mouse strains. With the indirect immunoferritin method, E antigen was seen in discrete patches on the surface of E+ leukemia cells. No murine leukemia virus (Type 1 or enveloped A) was observed in E+ leukemias. Although intracisternal A particles were present, it is unlikely that they are related to E antigen, since these particles are also found in - leukemias and solid tumors. Thus, it is not known whether E antigen originates from cellular or viral genes.

70-2352 TRANSMISSION OF SOME TUMOR VIRUSES. (E.) Mirand, E. A. (Roswell Park Mem. Inst., Buffalo, N. Y.) and A. G. Mirand. J. Surg. Oncol. 1(4):297-315, 1969.

It is concluded that the transmission of Friend leukemia virus (FLV), Rauscher leukemia virus (RLV) and 334C virus in male and female Ha/ICR Swiss mice is horizontal (transmission within a species by postnatal contact), but minimal under conditions prevailing in the natural environment. Foster-nursing experiments showed that the most effective transmission of FLV, RLV and 334C virus occurs through the mother's milk. Transplacental transmission of virus was not observed in reciprocal foster-nursing studies or in tests of embryo extracts from FLV and RLV-infected mothers, but tests of embryo extracts suggest that some transplacental transmission of 334C virus may occur. FLV and RLV were not transmitted through a paternal line, but the relatively high infectivity of semen and the low frequency of leukemia in litters sired by infected males suggest that 334C virus is very likely transmitted by a male parent. A low frequency of leukemia with a long latent period was obtained by inj. of urine from animals infected with FLV, RLV and 334C virus or inj. of oral washings and fecal preparations from mice infected with 334C virus. Leukemia was induced in 2/56 adult mice given a 1% extract from FLV-infected spleens as their drinking water for periods ranging from 12-120 days. This low incidence of leukemia may have been caused by inactivation of the virus either in the saliva or in the gut. Foodborne transmission of FLV or contact with animals infected

with FLV or RLV did not result in the development of leukemia.

70-2353 HOST-RANGE RESTRICTIONS OF MURINE LEUKEMIA VIRUSES IN MOUSE EMBRYO CELL CULTURES. (E.) Hartley, J. W. (NCI, Bethesda, Md.), W. P. Rowe and R. J. Huebner. J. Virol. 5(2):221-225, 1970.

On the basis of their ability to propagate in cells of NIH Swiss and BALB/c mouse embryos, murine leukemia virus strains have been classified into 3 groups: N-tropic, B-tropic and NB-tropic. Cultures of NIH cells were 100-1000-fold more sensitive to N-tropic strains (Friend, Gross passage A, AKR-L1, C3H/Fg-E1, C3H/He-E1, BALB/c-S1, BALB/c-S2N) than BALB/c cell cultures, but were only 1/30-1/100 as sensitive to B-tropic strains (BALB/c-T1, BALB/c-S2B, C57BL-MCT1). NB strains (Moloney, Rauscher, WMI-B) were propagated equally well in both cell lines. The same results were obtained whether virus was titrated by fluorescent-antibody focus assay, complement-fixation for murine leukemia or focus formation by Moloney sarcoma virus pseudotypes. It is concluded that the host range is under the genetic control of the virus, since no changes in tropism occurred when virus was passaged in resistant cells and no evidence of mixed virus populations was found. No correlation was seen between the host range and the Gross-AKR or FMR serotype.

70-2354 SPECIFIC SURFACE ANTIGEN FOR LEUKEMIA AND MALIGNANT TRANSFORMATION OF CELLS FROM CC57BR MICE INFECTED WITH MAZURENKO VIRUS. (Rus.) Gurtsevich, V. E. (Inst. Exp. Clin. Oncol., Moscow), N. P. Mazurenko, E. I. Zharova, N. A. Probatova and G. N. Stepanova. Biull. Eksp. Biol. Med. 69(3):100-104, 1970.

Specific surface antigen for Mazurenko leukemia virus (MLV) was detected by fluorescence microscopy in the spleens and brains of CC57BR mice, inj. (i.p.) 7 days previously with conc. MLV. From 10-13 days after infection, only spleen cells contained this antigen; beginning with day 15, the antigen was also found in the lymph nodes, thymus and bone marrow of these mice. The nature of this antigen is unknown, but it might be related to changes occurring in the cell surface during viral leukemogenesis. Changes characteristic of leukemia (large numbers of histiocytes, fibrocytes and reticulocytes in the spleen, liver and kidneys and large numbers of monocytes in the peripheral blood) became evident 22 days after inoc. When 1-1.5-mo.-old CC57BR mice were inj. i.p. with spleen cells from mice inj. with MLV 18 days previously, leukemia developed within 4-5 weeks.

70-2355 POSSIBLE SYNERGISM OF IRRADIATION AND VIRUS IN LEUKEMIA DEVELOPMENT. (Jap.) Yokoro, K. (Hiroshima U. Inst. Atomic Med., Japan). Saishin Igaku 24(11):2252-2255, 1969.

Leukemia developed in 21/34 ICR/JCL mice (61.8%) receiving ^{90}Sr (1.0 $\mu\text{C/g}$ body wt., i.p.). The development of leukemia was not inhibited by thymectomy (thmx.) in 24/34 (70.6%) mice receiving ^{90}Sr . Leukemia developed in 17/22 mice (77.3%) admin. X-irradiation (600 r; 4 admin.) and was inhibited in 7/24 mice (29.2%) which received X-irradiation + thmx. When W/Fu rats were inoc. i.p. with Gross leukemia virus (GLV) after X-irradiation (as above), 11/20 (55%) developed leukemia; all 15 young rats receiving GLV alone developed leukemia. The leukemia was thymic lymphoma in all cases. Synergism between irradiation and virus in the development of leukemia is suggested.

70-2356 TRANSFORMATION AND VIRUS PRODUCTION IN NORMAL RAT THYMUS CELLS AND THOSE INFECTED WITH MOLONEY LEUKEMIA VIRUS. (E.) Cremer, N. E. (California State Dept. Public Health Viral Rickettsial Dis. Lab., Berkeley), D. O. N. Taylor, L. S. Oshiro and Y. Teitz. *J. Nat. Cancer Inst.* 45(1):37-48, 1970.

Cultures of thymus cells from 2-3-day-old Osborne-Mendel (O/M) rats were inoc. with Moloney leukemia virus (MLV) and designated as cell lines T21M and T24M (T21C and T24C were controls). A fluctuation in brilliance and amount of staining with rat fluorescein-labeled anti-MLV antibody was seen over a period of 3 yr. Inj. of T21M and T21C cells into O/M rats of various ages (newborn-1 mo.) induced fibrosarcomas and reticulum cell sarcomas at the site of inj. in 9/16 and 3/16 rats, resp. No rats inj. with either infected or control T24 cells developed tumors at inoc. site. Adult or weanling rats developed no tumors when inoc. with either cell line. Thymic lymphomas developed after T21M or T24M inoc., presumably as a result of MLV virus present in the cell inocula.

70-2357 BIOLOGIC AND MORPHOLOGIC ANALYSIS OF GROWTH AND CELLULAR PATTERN OF TISSUES FROM MICE WITH VIRAL LEUKEMIA CULTURED IN VITRO. (E.) Niezabitowski, A. (Med. Acad., Cracow, Poland). *Acta Med. Pol.* 10(4):389-400, 1969.

Tissue cultures were made from the spleen, lymph nodes, bone marrow and thymus of inbred XVII B1n mice with various forms of leukemia induced by Graffi virus. The growth rate of these cultures was apparently related to the form of leukemia and was slower in spleen and lymph node cultures than in bone marrow and thymus cultures. In tissue cultures from mice with chloroleukemia and myeloid leukemia the growth rate was faster than in tissue cultures from mice with erythro-leukemia, reticulocytic leukemia or mixed forms of leukemia. Differences in the cytological patterns of these cultures were related to the form of leukemia and the type of tissue. Cytological patterns were more diversified in chloroleukemia and myeloid leukemia and in spleen and lymph node cultures. There is no evidence

to indicate whether these cells are leukemia cells or normal cells which have been transformed in vitro. Lymphocytic phagocytosis, observed in some cultures, suggests that the cells are hematopoietic in origin.

70-2358 MURINE SARCOMA AND LEUKEMIA VIRUSES: ASSAY USING CLONAL LINES OF CONTACT-INHIBITED MOUSE CELLS. (E.) Jainchill, J. L. (NCI, Bethesda, Md.), S. A. Aaronson and G. J. Todaro. *J. Virol.* 4(5):549-553, 1969.

A continuous cell line of highly contact-inhibited cells (NIH/3T3) was developed from NIH Swiss mouse embryo cultures. Its properties, which make it very suitable for the study of viruses of the murine sarcoma-leukemia (MS-L) complex, are similar to those of 3T3 and BALB/3T3. NIH/3T3 cells were about twice as sensitive as the original 3T3 to SV40 transformation. Complement fixation and fluorescent antibody tests showed no evidence of the MS-L complex. Even after long periods of culture, NIH/3T3 retained the sensitivity and specificity of the original NIH Swiss mouse embryo cells to the MS-L complex. This specificity may be attributed either to an absorption block or to intracellular restriction of viral replication. When infected with "Swiss-tropic" murine sarcoma virus (MSV: obtained as the Moloney concentrate), about 3-fold as many foci formed in NIH/3T3 cells as in NIH Swiss embryo cells, and about 100-fold as many foci formed in NIH/3T3 cells as in the original 3T3 line. NIH/3T3 and NIH embryo cells were almost equal in their sensitivity to "Swiss-tropic" leukemia virus. MSV-transformed NIH/3T3 lines were not contact-inhibited and grew to a high saturation density. They also released large amounts of NIH "Swiss-tropic" MSV and leukemia virus into the medium.

70-2359 REPLICATION OF DEFECTIVE AND COMPETENT FORMS OF MURINE SARCOMA VIRUS IN MOUSE CELL CULTURES. (E.) Fischinger, P. J. (NCI, Bethesda, Md.) and T. E. O'Connor. *Virology* 41(2):233-243, 1970.

Propagation of the constituents of the Moloney murine sarcoma-leukemia complex was investigated in 3 different cell culture systems derived from Swiss mice (Swiss mouse embryo fibroblasts, the 3T3 cell line, and secondary neonatal Swiss mouse kidney cultures) to determine whether a particular cell system could affect the composition of the viral complex. Defective and competent murine sarcoma virus (MSV) and murine leukemia virus (MLV) were adsorbed to the same degree on all 3 cell types. MLV alone grew well in mouse embryo cultures, poorly in the 3T3 cell line, and very poorly in the kidney cultures. A mixture of defective MSV and MLV grew rapidly in embryo cultures and eventually yielded some competent MSV progeny. This mixture grew poorly in the 3T3 cell line and virus was

st barely detected in the kidney cultures. The slow growth rate of defective MSV in 3T3 cells was not enhanced by addition of exogenous V. Virus consisting primarily of competent V grew rapidly and well in all 3 cell systems. Both competent and defective MSV were obtained in progeny from competent MSV in 3T3 cells. When 3 cells were inoc. with competent MSV, defective virus was produced initially and was followed by the production of competent MSV. In mouse kidney cells competent MSV produced primarily defective MSV, small amounts of competent MSV and very little MLV.

2360 VIRUS-SPECIFIED CHANGES IN THE SUGAR-TRANSPORT KINETICS OF RAT EMBRYO CELLS INFECTED WITH MURINE SARCOMA VIRUS. (E.) Tanaka, M. (Flow Labs. Inc., Rockville, Md.) and R. V. Gilden. J. Nat. Cancer Inst. 45(1):1-89, 1970.

Cultures of rat and hamster embryo cells (EC), human embryonic kidney cells and WI-38 cells were inoc. with Harvey sarcoma virus (HSV; 10^4 i.u.). Only the rat EC were transformed by HSV. Sugar transport by hamster and human EC showed no change over a 20-day period, whereas rat EC showed an altered sugar transport after 8 days. Results were the same as for HSV-infected mouse cells. Uptake of D-glucose, D-mannose, D-lactose and 2-deoxy-D-glucose was enhanced, while uptake of 3-O-methyl-D-glucose was unchanged or slightly reduced. It is suggested that altered sugar transport kinetics in HSV-infected cells are virus-specified.

2361 THE BEHAVIOUR OF TWO STRAINS OF MURINE SARCOMA VIRUS IN VITRO. (E.) Simons, P. J. (U. Western Australia, Perth). Aust. J. Biol. Med. Sci. 48(1):105-114, 1970.

Moloney sarcoma virus (MSV)- and Harvey sarcoma virus (HSV)-infected cell cultures were studied for transformation by virus. By 44 hours after infection, growth rate was reduced in both virus-infected cultures as compared to CL-1 (BALB/c mouse embryo fibroblasts) controls. From 44-78 hours, the MSV culture growth rate increased, but by 144 hours the HSV culture had half the number of cells as controls. MSV produced round and spindle cells which were overgrown by normal cells on further passage, whereas, after HSV infection, they multiplied in subculture. HSV produced multinucleate giant cells and the HSV-transformed cells formed colonies in soft agar; pure lines were, thus, established.

2362 PRESENCE OF UNUSUAL VIRUS PARTICLES IN TWO HAMSTER TUMOUR TISSUE CULTURE LINES INDUCED BY MURINE SARCOMA VIRUS. (E.) de Petris, S. (Nat. Inst. Med. Res., London) and J. Harvey. J. Gen. Virol. 5(4):561-564, 1969.

Comparative electron microscopic study of 2 tissue culture lines of hamster tumor cells (B34 induced by Harvey sarcoma virus and 8303 cells induced by Moloney sarcoma virus) showed no Type C particles resembling murine leukemia virus in either cell line. Many cells of both cultures contained intracytoplasmic and unusually spoke-shaped, virus-like particles. These particles were enclosed by small vacuoles which had ribosomes on their membranes. Single and budding particles appeared similar, with a mean external diameter of 1000 Å and surrounded by a 3-layer membrane.

70-2363 PATHOGENESIS OF VIRUS-INDUCED MURINE SARCOMA. I. LIGHT MICROSCOPY. (E.) Siegler, R. (Boston U. Sch. Med., Mass.). J. Nat. Cancer Inst. 45(1):135-147, 1970.

Random-bred Ha/ICR Swiss albino mice received a single s.c. inj. of either Harvey or Moloney murine sarcoma virus (MSV) and the skin of the back at the site of inj. was studied histologically in mice sacrificed for the next 28 days. Local lesions with Harvey and Moloney isolates were indistinguishable. Within 2 days of inj. there were grossly visible inflammatory reactions which formed a palpable mass by day 5, when most of the inflammatory cells were lymphocytes and macrophages. At days 7-10, most specimens showed a granuloma-like lesion, with angiomatoid proliferation of capillary endothelium and necrosis of striated muscle. At days 10-14 there were proliferative (sarcomatous) changes with the initial fluid in the mass being replaced by fibroblast proliferation. The last phase was tumor regression, which progressed somewhat differently for small and large masses.

70-2364 LIGHT AND ELECTRON MICROSCOPE STUDIES OF OSTEOSARCOMAS INDUCED IN RATS AND HAMSTERS BY HARVEY AND MOLONEY SARCOMA VIRUSES. (E.) Fujinaga, S. (U. Texas M. D. Anderson Hosp. Tumor Inst., Houston), W. E. Poel and L. Dmochowski. Cancer Res. 30(6):1698-1708, 1970.

Histological and ultrastructural study of osteosarcomas induced in NZB rats and golden Syrian hamsters by i.p. inj. of Moloney or Harvey murine sarcoma virus (MSV) showed that tumors were multicentric, periosteal and predominantly osteogenic in both species. In contrast to localized tumors and other reactions obtained by s.c. or i.m. inoc. of MSV, the multifocal origin of these tumors suggests a systemic infection resulting in multiple primary neoplasms. The tumors contained areas of osteolytic, chondrogenic, angiosarcomatous, histiocytic and mesenchymal cell proliferation as satellite growths in the surrounding parenchyma. Invasion of the marrow space and adjacent skeletal muscle by malignant osteoblasts, anaplastic sarcoma cells, and multinucleated giant cells was common.

Large numbers of budding, immature and mature virus particles, morphologically identical with murine leukemia Type C particles, were found in rat tumors induced with Moloney MSV. Few mature Type C particles were found in hamster tumors induced with either Moloney or Harvey MSV. A difference of host reaction to the virus may be a factor responsible for this difference. Type C particles were also present in tissue culture cells derived from the primary osteosarcomas. Bernhard Type H particles were found in hamster osteosarcomas and their cultures; the significance of these particles is unknown. The induction of osteosarcomas in animals of more than 1 species provides another indication of the lack of target specificity and species specificity of oncogenic viruses.

70-2365 INVESTIGATION OF THE SENSITIVITY OF VARIOUS LABORATORY ANIMALS TO MOLONEY SARCOMA VIRUS. (Rus.) Kukain, R. A. (Kirkhenshtein Inst. Microbiol., Riga, USSR), L. I. Nagaeva, R. K. Eligulashvili and S. V. Chapenko. Vop. Virus. 14(3):305-309, 1969.

Cell-free extracts of strain 221 of Moloney sarcoma virus (MSV), which had been passaged in BALB/c mice, were inj. i.m. into noninbred and BALB/c mice (1 day-2 mo. old), newborn Wistar rats, noninbred rabbits, guinea pigs, Syrian hamsters and chicks. Tumors developed in both noninbred and BALB/c mice and in Wistar rats. The polymorphic rhabdomyosarcomas, which developed in 90-95% of the newborn BALB/c mice, had very short incubation periods and never regressed in mice aged 1-3 days. When these mice were 10 days old or older at inoc., only 50% developed tumors, the incubation period increased to 2 weeks, and all of the tumors regressed. Most mice with tumors had WBC counts 5-8-fold greater than normal. The WBC decreased when the tumors regressed. After an incubation period of 60-135 days, 27/160 (17%) infected Wistar rats developed tumors which progressively increased in size so that they accounted for 50-60% of the body wt. at death. Symptoms of lymphatic leukemia were observed in 6/27 rats. Cell-free extracts from these rat tumors induced tumors in BALB/c mice. Generalized involvement of the lymphatic system and tumors in the lungs, pancreas, thymus and spleen were noted in 9 rats. An additional 12 rats, which had no evidence of tumors, exhibited enlargement of the spleen, liver and lymph nodes and severe anemia.

70-2366 DEPENDENCE OF MURINE SARCOMA VIRUS INFECTION ON THE CELL CYCLE. (E.) Yoshikura, H. (Nat. Inst. Health, Shinagawa-ku, Tokyo). J. Gen. Virol. 6(1):183-185, 1970.

Studies of synchronous cell division induced in the C3H2K line (from newborn C3H/He mouse kidney) by scraping a confluent monolayer of cells indicated that max. DNA synthesis occurred at 20

hours after scraping. Mitosis occurred after 30 hours in the area of the defect. In C3H2K monolayers infected with Moloney sarcoma virus 20 hours after scraping, transformed cells appeared only in the scraped area, while no clear transformed area appeared when the cells were infected just after scraping or after 40 hours. This indicates that the virus did not induce, but was dependent upon, cell replication.

70-2367 THE RESPONSE OF NZW X NZB F₁ HYBRID MICE TO A MURINE SARCOMA VIRUS. (E.) Gazdar, A. F. (NCI, Bethesda, Md.). Int. Arch. Allerg. 38(5):509-513, 1970.

Initial tumor appearance and regression in 4-6-week-old NZW/B F₁ hybrid mice infected with Moloney sarcoma virus was quite similar to that reported for C3H/HeN, AL/N, N:GP(SW), C57BL/6N, AKR/N, DBA/2N and BALB/cCr. The NZB/W F₁ mice failed to develop recurrent tumors. Older NZB/W F₁ hybrids with proteinuria did not show the immunological over-reactiveness seen in the 4-6-week-old mice, and showed a decreased frequency of tumor regression with a similar increase in the development of tumor recurrences.

70-2368 CYTOLOGIC SPECIFICITY OF RESPONSE TO MOLONEY MURINE SARCOMA VIRUS AS EVIDENT IN A TRANSPLANTABLE EPITHELOID NEOPLASM OF THE RAT. (E.) Stanton, M. F. (NCI, Bethesda, Md.), R. C. Ting and E. Miller. J. Nat. Cancer Inst. 45(1):195-209, 1970.

Morphological features and ultrastructure of MSB-1, a transplantable tumor which was induced in a thymectomized female BN rat by inj. of a cell-free extract from tumors produced by Moloney sarcoma virus (MSV), are presented. When inj. s.c. into BN rats, these cells did not produce the local or disseminated granulomatous lesions characteristic of Moloney sarcoma. The tumors were composed entirely of cells unrelated to adjacent tissues, but most likely originated from the mammary epithelium. The tumor cells were large and polygonal and were arranged in a pavement-like structure. The nucleoplasm contained 2 different types of granular deposits, 1 of which was similar to "dense bodies" described in human mammary tumors and in chicken fibroblasts infected with Rous sarcoma virus. Both mature and immature type C particles characteristic of murine sarcoma and leukemia viruses were distributed sparsely in the intercellular spaces, and mature particles were found in cytoplasmic vacuoles. Budding occurred from the plasma membrane in only 3/53 cases and from the intracytoplasmic membranes in 3 cases. It is possible that the change which occurred in MSV represents a gene-linked change in response to the introduction of Type C RNA viruses. The presence of free virus, however, indicates that the change may be an epigenetic phenomenon even though it is related to viral invasion.

-2369 RESCUE OF DEFECTIVE MURINE SARCOMA VIRUS GENOME FROM 50 CLONES OF A NON-PRODUCER HAMSTER TUMOUR CELL LINE. (E.) Chang, S. (Flow Labs. Inc., Rockville, Md.), R. J. ... ni, R. V. Gilden, M. Hatanaka and R. J. Huebner. Gen. Virol. 5(3):443-445, 1969.

Sarcoma virus was rescued from 50/50 clones of 11 line HT-1, derived from a hamster tumor induced by Moloney sarcoma virus. The rescue procedure involved cocultivation of 8×10^4 HT-1 cells with 8×10^5 cells of a mouse cell line which produced leukemia. Sarcoma virus from disrupted cells was recovered after 1 week of incubation at 37°C . Sarcoma virus was also recovered from 9/9 clones by a conventional method (not further specified). Yields of virus were almost the same, an av. of 10^3 FFU/culture. 11 line HT-1 had previously been shown to contain no infectious virus, noninfectious particles, or group-specific antigen for Type C A virus in the complement fixation test.

-2370 IMMUNOSUPPRESSION BY MURINE SARCOMA VIRUS (MOLONEY). (E.) Chan, S. P. ... ionetics Res. Labs., Bethesda, Md.), W. A. ... k, W. Turner and M. A. Chirigos. Infection and Immunity 1(3):288-292, 1970.

Infection of BALB/c mice with Moloney sarcoma virus (MSV) markedly suppressed the humoral antibody response to sheep RBC (inj. i.p.), both 5 days after MSV infection (when tumor size had reached a max.) and 26 days after infection (when primary tumors had partially regressed). 10-fold reduction in hemolytic antibody titer was observed in mice with primary, regressed and current tumors. Cellular immune response, as manifested by rejection of allografts, was significantly reduced in BALB/c mice infected with MSV 5 days before grafting. The median survival time of skin grafts from C3H mice was 14 days longer than in noninfected controls. The median graft survival time was increased only 4 days when grafts were made in mice with large primary tumors or recurrent tumors and metastases. Moloney leukemia virus (MLV), present as a contaminant in MSV preparations, significantly reduced humoral antibody response to sheep RBC antigen when mice were immunized 25 and 49 days after MLV infection; no detectable signs of MLV-induced disease were observed in these animals. MLV had no effect on cellular immune response in mice, indicating that this contaminant is not solely responsible for depression of cellular immune response induced by MSV.

70-2371 THE PATHOGENIC ACTION FOR MICE OF PHENOLIC EXTRACT (RNA) FROM FOWL SARCOMA INDUCED BY THE CARR (ZILBER) STRAIN OF SARCOMA VIRUS. (E.) Nastac, E. (St. S. ... lau Inst. Inframicrobiol., Bucharest), M. ... u, P. Athanasiu, E. Ciufecu and M. Stoian. Roum. Inframicrobiol. 6(4):295-300, 1969.

Newborn, pregnant and adult white mice admin. a phenolic RNA extract from fowl sarcoma induced by the Carr (Zilber) strain of Rous sarcoma virus, developed general hypertrophy of the lymph nodes, solid tumors under the skin or in the lungs and marked hepatosplenomegaly after 5-16 mo. In all cases nucleic acid extract activity was inhibited by pretreatment with RNase. RNA extracted from these mouse tumors induced tumors on the chorioallantoic membrane of sarcoma-free chick embryos.

70-2372 CHARACTERISTICS OF VARIANTS OF ROUS SARCOMA VIRUS (RSV) ISOLATED FROM MOUSE RSV TUMORS. (E.) Kryukova, I. N. (Gamaleya Inst., Moscow), I. B. Obukh and F. Tot. J. Nat. Cancer Inst. 45(1):49-57, 1970.

Tumors induced by inj. of adult mice with nontransformed syngenic mouse embryo tissue culture, which had been exposed to the Carr-Zilber (C-Z) strain of Rous sarcoma virus (RSV), were homogenized and several mouse variants of RSV isolated. These variants of RSV had highly oncogenic effects in adult mice and produced less foci (pocks) of transformation on chick embryo chorioallantoic membranes (CAM). All but 1 mouse variant had coat antigen identical to that for the C-Z strain. Pocks of various shapes were produced, and several different types were highly oncogenic in adult mice. The C-Z strain and the Schmidt-Ruppin strain of RSV (non-oncogenic in adult mice) both developed oncogenic activity in adult mice after passage through CAM of chick embryos.

70-2373 TUMOR INDUCTION IN ADULT RATS WITH ROUS SARCOMA VIRUS. 2. VIROLOGICAL AND ANTIGENIC PROPERTIES OF PRIMARY AND TRANSPLANTED TUMORS FROM ADULT RATS. (Rus.) Kuznetsova, N. N. (N. F. Gamalei Inst. Epidem. Microbiol., Moscow), V. Ia. Shevliagin and T. I. Biriulina. Vop. Virus 15(1):47-52, 1970.

On the basis of virological and immunological studies, 40 primary tumors induced in adult Wistar rats with Rous sarcoma virus (RSV; Schmidt-Ruppin strain) and 7 tumors passaged first in adult August rats were classified into 4 groups. Group (1) tumors, found in 2/40 Wistar rats after 15 and 20 days, contained mature RSV and 35% and 68% of the tumor cells, resp., contained viral antigen. Typical Rous sarcomas were produced in White Leghorn chicks by inj. of cell-free extracts from these tumors. Virus-neutralizing antibodies were present in sera from these rats. Group (2) tumors developed in 19/40 Wistar and in 7/7 August rats after latent periods of 1-5 mo. All of these tumors contained virus bound to the cells, and 8/19 contained viral antigens in 26-42% of the cells. Cell-free extracts from these tumors did not produce tumors in chicks, but inj. of untreated tumor cells did. Virus-free group (3)

tumors developed in 8/40 Wistar rats after latent periods of 15-30 days. Neither cell-free extracts nor untreated cells from these tumors produced Rous sarcoma in chicks. Viral synthesis, however, was activated by the artificial heterokaryon method but not by X-irradiation (5000-10,000 r). Viral group-specific (gs) antigens were found in 47% of group (2) and (3) tumors by the fluorescent antibody (FA) method and in 17% by the complement-fixation (CF) test; gs-antibodies were found in sera of 29% of these rats. Virus-free group (4) tumors developed in 11/40 Wistar rats after a latent period of 3 mo. Viral gs-antigens were found in 1/11 tumors with the CF test and in 0/11 tumors with the FA method. No virus-neutralizing or CF gs-antibodies were found in the sera of any of these animals.

70-2374 VIRUS-SPECIFIC ANTIGENS IN HAMSTER CELLS TRANSFORMED BY ROUS SARCOMA VIRUS. (E.) Fleissner, E. (Sloan-Kettering Inst., New York, N. Y.). J. Virol. 5(1):14-21, 1970.

Hamster cells were transformed *in vivo* by Bryan high-titer strain of Rous sarcoma virus (RSV) and examined for production of virus. No infectious virus or RSV-like particles were found after growth in chick embryo cells or electron microscopy, and no avian leukosis group-specific antigen was seen. Fluorescent antibody staining methods and complement fixation (CF) after subcellular fractionation showed virus-specific antigens concentrated at discrete loci exclusively in the cytoplasm. Velocity and isopycnic centrifugation showed CF antigen to be soluble, or in association with membranes and polyribosomes. The antigens were immunologically identical to proteins released, after ether treatment, from RSV-related viruses.

70-2375 ELECTRON MICROSCOPE STUDY OF CELLS FROM TUMORS INDUCED IN HAMSTERS BY ROUS VIRUS, AFTER LONG-TERM PASSAGE *IN VITRO*. (Rus.) Kupchinskii, L. G. (Biophys. Inst., Moscow), V. M. Mitushin and V. Ia. Shevliagin. Vop. Onkol. 16(4):86-90, 1970.

Electron microscope study of a clone (clone #9) of tumor cells induced in hamsters by Rous sarcoma virus, which never formed a monolayer on glass and had a "migrating" growth pattern, showed mitochondria with randomly oriented, tubular cristae. Mitochondria such as these were previously described in cells from the central nervous system of rats and mice, in cells from the adrenal cortex and in a number of protozoa, but this is the first time they have been seen in transplantable cultures of mammalian cells. The ultrastructure of the nucleus, irregular in shape, was characteristic of cells with an active metabolism. Apparently the nuclear membrane serves both to isolate the nucleus from the cytoplasm and to provide an

effective link between the nucleus and cytoplasmic components. The fibrillar formations also observed suggest an inherent contractile ability.

70-2376 RESISTANCE OF CHICK EMBRYO CULTURES TO ROUS VIRUS. (Rus.) Diad'kova, A. M. (N. N. Petrov Sci. Res. Inst. Oncol., Leningrad, USSR), O. K. Kuznetsov, K. P. Romanov and G. I. Goloviznin. Vop. Onkol. 14(11):56-61, 1968.

Chick embryo cell cultures, obtained by simultaneous trypsinization of 60-90 embryos, were 100-10,000-fold more resistant to the Bryan strain of Rous sarcoma virus (RSV) than sensitive control cultures by generation 3. Medium taken 4-7 days after transferring generation 4 of RSV-resistant cells induced resistance in highly sensitive cultures of chick fibroblasts. The rate at which this resistance developed was directly proportional to the conc. of the medium used. Complement-fixing (CF) antibodies to RSV were detected in titers of 1:40-1:320 in medium from both RSV-resistant and RSV-sensitive chick embryo cultures, indicating that soluble CF antigens are present. The fluorescent antibody test demonstrated that in RSV-resistant, but not in RSV-sensitive, cultures, antigen accumulated in the cytoplasm, later appeared in the cell membrane, and was finally liberated from the cells. These findings confirmed previous reports that the RSV-inhibiting factor is identical with lymphogenous leukemia virus.

70-2377 INCORPORATION OF PRECURSORS INTO RIBONUCLEIC ACID, PROTEIN, GLYCOPROTEIN, AND LIPOPROTEIN OF AVIAN MYELOBLASTOSIS VIRIONS. (E.) Baluda, M. A. (U. California Sch. Med., Los Angeles) and D. P. Nayak. J. Virol. 4(5): 554-566, 1969.

Myeloblasts obtained from the blood of chicks infected in embryo with BAI strain A avian myeloblastosis virus (AMV), synthesized AMV *in vitro* at a constant rate without any apparent cytopathic effect. A study of the kinetics of ³H-uridine incorporation revealed that 3-4 hours elapsed between the time viral RNA was synthesized and the time it was released as a mature viral particle; this represents the av. time interval spent by AMV-RNA in an intracellular pool. Studies of ¹⁴C-phenylalanine incorporation showed that some protein synthesis occurs at or near the cell surface immediately before viral maturation and release. ¹⁴C-glucosamine also appears to be incorporated into the outer viral envelope shortly before maturation, but there is an av. time lag of 16-20 hours before most of the ¹⁴C-ethanolamine, incorporated into intracellular lipoprotein, appears in the free virions. This delay probably represents the time interval required by newly synthesized membrane lipids to reach the cell surface where

AMV matures. These findings suggest that synthesis of viral lipoproteins might be the limiting step in the 14-20 hr. latent period established for AMV. Actinomycin D inhibits viral RNA synthesis within 30 min. but permits MV to mature for at least 2 hours. AMV released in the presence of actinomycin D contains viral RNA synthesized before addition of the antibiotic.

0-2378 DNA COMPLEMENTARY TO VIRAL RNA IN LEUKEMIC CELLS INDUCED BY AVIAN MYELOBLASTOSIS VIRUS. (E.) Baluda, M. A. (U. California Sch. Med., Los Angeles) and D. P. Nayak. Proc. Nat. Acad. Sci. USA 66(2):329-336, 1970.

From RNA-DNA hybridization studies, evidence was obtained to support the hypothesis that avian myeloblastosis virus (AMV) replicates its RNA genome by a DNA intermediate. The 71S component of AMV-RNA hybridized specifically with the DNA from the myeloblasts of leukemic chickens and, to a lesser extent, with DNA from normal chick embryos. DNA from leukemic chicks hybridized about 2-fold as much viral RNA as did DNA from normal chicken embryos. This could result either from a natural homology between viral DNA and chicken DNA or from contamination of the chick embryos by some avian leukosis virus partially homologous to AMV. The latter hypothesis is suggested by the finding that about 10% of the chick embryos used in this study developed spontaneous leukosis. Thermal melting studies revealed that the viral RNA bound to normal and leukemic DNA consists of long polynucleotides ($T_m = 87^\circ$ and 92° C, resp., in 0.5M saline citrate). The heat stability and high melting values of these hybrids indicate that sequences of at least 100 nucleotides are involved and that extensive homology between the 2 nucleic acids is not due to accidental similarities.

7-2379 CLAUDE'S CHICKEN TUMOR VIRUS-10: LOCAL VARIABILITY IN VIRUS TITER AND EFFECT OF AMPUTATION. (E.) Hewetson, J. F. (Karolinska Inst., Stockholm) and V. Groupé. Cancer Res. 36(17):1743-1747, 1970.

Sarcomas were produced in the wing-web of chickens by s.c. inj. of serial dilutions of Claude's chicken tumor virus 10 (CTV-10) into the wing web of 1-3-day-old White Leghorn chicks, and the infectious virus assayed. Infectivity titers varied greatly, both between portions of the same tumor and among tumors from birds in the same dose group. No clear relationship was seen between the virus yield and the dose used to induce tumors. Amputation of the infected wing 0-4 hours after s.c. inoc. of CTV-10 did not prevent tumor development at the stump or prolong survival of the bird. These stump tumors did not develop in infected birds in which the

uninfected wing was amputated. Thus, close proximity of the amputation to the site of infection is necessary for tumor development. Development of the tumor preceded the appearance of titratable virus. The latent period was prolonged by i.m. inj. of CTV-10 hyperimmune serum 1 day before, but not 1 day after, s.c. inoc. with CTV-10. The latent period was essentially the same for male and female chicks.

70-2380 IMMUNOFLOUORESCENCE AND ELECTRON MICROSCOPE DETECTION OF VIRUS PARTICLES IN TISSUE CULTURES INFECTED WITH ROUS SARCOMA VIRUS. (Rus.) Diad'kova, A. M. (N. N. Petrov Sci. Res. Inst. Oncol., Leningrad, USSR), O. K. Kuznetsov and G. A. Savost'ianov. Vop. Onkol. 16(5):65-72, 1970.

Rous sarcoma virus (RSV) was detected in monolayers of chick embryonic fibroblasts 1 day after infection with 10^2 - 10^5 FFU/ml of strain D. The virus was found at a lower titer in the culture fluid 2 days after infection. The virus titer reached a max., both in the cells and culture fluid, 5-6 days after infection, after which it remained unchanged. Immunofluorescence studies showed that virus antigen was present in the perinuclear zone 1 day after infection. This antigen later filled the entire cytoplasm and was also found on the fibroblast surface. Electron microscopy revealed that 2 types of particles were present. One was characteristic for RSV and was found on the cell surface, in pinocytotic vacuoles or as small vacuoles located on the cell surface or deep in the cytoplasm. In a few cases these particles were observed entering the cell. Oval particles, 50-70 mμ in diameter, were found in the cytoplasm or sometimes on the cell surface. These particles, the nature of which is unknown, were not found in noninfected chick fibroblast cultures. It is suggested that they are either precursors of the typical virus particles or a result of their abortive synthesis.

70-2381 RADIO-INDUCED MUTANTS OF THE SCHMIDT-RUPPIN STRAIN OF ROUS SARCOMA VIRUS. (E.) Goldé, A. (Radium Biol. Inst., Orsay, France). Virology 40(4):1022-1029, 1970.

In a study of pock cultures, the virus-producing capacity of clonal and subclonal Schmidt-Ruppin strain of Rous sarcoma virus (SR-RSV) irradiated with ^{60}Co showed a 0-25% increase of nonproducing (NP) transformed cells as irradiation dosage increased. Of those focus cultures that remained virus-producers, the smaller virus yield occurred at higher irradiation dose. NP cells, obtained by inoc. of irradiated viral suspensions either on the chorioallantoic membrane (CAM) or on chicken cells *in vitro*, induced graft tumors on the egg CAM. A group of mutant virions, which were unable to transform C/O chick embryo cells, but

were able to replicate at high titer and induce high group specific antigen levels, were obtained. This mutant confers to the cells a high resistance against RSV challenge (subgroups B and D of avian oncogenic viruses), and a slight resistance against subgroup A RSV challenge. The hypothesis of the independence of oncogenic and virus-producing capacities is reaffirmed.

70-2382 SEROLOGICAL STUDY OF THE EPIDEMIOLOGY OF INFECTIOUS AND ONCOGENIC AVIAN VIRUSES IN SOME SPECIES OF WILD AND DOMESTIC BIRDS. (Rus.) Voronin, E. S. (L. A. Tarasevich State Control Inst. Med. Biol. Preps., Moscow), S. G. Dzagurov, N. E. Smirnova, K. V. Morozov and K. A. Elekoev. Vop. Virus. 15(2):213-217, 1970.

Virus-neutralizing antibodies for a variety of strains of Rous sarcoma virus (RSV) were measured in sera from Japanese quail, ducks, wild pigeons, sparrows and chickens. These antibodies were found in rather large percentages of domestic fowl. Of the chickens, 40% had antibodies for the Bryan strain, 15% for the Schmidt-Ruppin strain, 10% for the Engelbreth-Holm strain, 11% for the Carr strain, 3% for the Brian C strain and 10% for the APL-22 strain of RSV. Virus-neutralizing antibodies for the Bryan strain were found in 28% of the Moscow chickens, in 40% of the White and Brown Leghorns, in 15% of the 3-mo.-old chicks and in 12% of the wild pigeons. None of the 1-day-old chicks, ducks or sparrows had virus-neutralizing antibodies for this strain of Rous sarcoma virus. Serological studies of Japanese quail from 3 farms showed that birds from 2 of these farms had no evidence of antibodies for Brian, Schmidt-Ruppin or Carr strains of RSV. Of the quail from the other farm, 44% had antibodies for the Bryan strain, 8% for the Schmidt-Ruppin strain and 10% for the Carr strain; this is attributed to the proximity of this farm to poultry-raising farms.

70-2383 REPTILE TUMORS AND CYSTS INDUCED WITH CHICKEN SARCOMA VIRUS. (Rus.) Veskova, T. K. (Inst. Exp. Clin. Oncol., Moscow), L. P. Trubcheninova and I. L. Duk. Vop. Virus. 15(2):217-220, 1970.

Different reptile and amphibian species were inj. with 0.2×10^5 - 5×10^6 sarcomatous doses of chicken sarcoma virus (CSV; Schmidt-Ruppin strain) and with WBC from pts. with leukemia. Adult and newly hatched animals were inj. s.c., i.m., i.p. and, in some cases, intracerebrally. A spindle-cell sarcoma was found in the thorax of Eremia velox 1.5 mo. after i.m. and i.p. inj. of CSV. Submaxillary cysts were found in 2-week-old boa constrictors (Erix tataricus) 1.5 mo. after i.m. and i.p. inj. of CSV. Polymorphocellular sarcomas developed in the peritoneum 1 yr. and 4 mo. after this species was inj. twice (route unspecified) with an interval of 2

mo. between inj. Two thin-walled hemorrhagic cysts were found in the trachea of 1/2 specimens of Natrix tessellata 25 days after infection with CSV. Cartilaginous proliferation was found in the bones of the extremities and digits of a gecko 252 days after infection with CSV. CSV had no effect on adult specimens of Natrix natrix, Agama sanguinolenta, A. erythrogastra, Varanus griseus, Eumeces scutatus, or Eremias persica. No tumors nor leukemia were seen during an 8-mo. observation period in 3-mo.-old axolotls inj. i.v. and i.p. with WBC from pts. with leukemia. No abnormalities were noted in 30 specimens of Eremias velox, 4-5-yr.-old tortoises (Testudo horsfieldii), Varanus griseus, or 2-week-old and adult boa constrictors (Erix tataricus), after inj. of leukemic human WBC.

70-2384 FUNCTION OF THE GENOME OF INACTIVATED SENDAI VIRUS IN THE FORMATION OF ARTIFICIAL HETEROKARYONS. (Rus.) Shliankevich, M. A. (Inst. Exp. Clin. Oncol., Moscow), L. B. Mekler and V. Ia. Shevliagin. Vop. Onkol. 16(1): 58-63, 1970.

When cultures of hamster Rous sarcoma cells and primary chick fibroblasts were inoc. with Sendai virus inactivated by UV-irradiation or by addition of 0.1% β -propiolactone, only T antigen formation was induced in the cells. No biosynthesis of V antigen, hemagglutinins, ribonucleoprotein or complete infectious virus occurred. The observation of V antigen fluorescence can be accounted for by the presence of virus particles in the cytoplasm and on the cell surface, but V antigen was not synthesized de novo. Inactivated Sendai virus was not reactivated by 5-7 passages made at 2-3 day intervals, indicating that the cells were completely virus-free. T antigen was found in both ordinary cells and heterokaryons for a short time but disappeared after 5-7 days. T antigen was not observed on the surface of cells inoc. with either infectious or inactivated Sendai virus. Apparently, antigenic changes in the cytoplasmic membranes which lead to artificial heterokaryon formation are due to the induction of another antigen which might be analogous in structure to Sendai virus antigen. The roles of cellular membranes in carcinogenesis are considered briefly.

70-2385 A CELL-ASSOCIATED FACTOR ESSENTIAL FOR FORMATION OF AN INFECTIOUS FORM OF ROUS SARCOMA VIRUS. (E.) Hanafusa, H. (City New York Public Health Res. Inst., N. Y.), T. Miyamoto and T. Hanafusa. Proc. Nat. Acad. Sci. USA 66(2):314-321, 1970.

Rous sarcoma virus (RSV)-infected chick embryo cells with no evidence of avian leukosis virus (ALV) appeared to have a genetic factor essential for the formation of infectious RSV(0). Infection with RSV or ALV grown in factor-containing

cells was used to convert factor-deficient cells to the infectious RSV(0) form. It is suggested that the factor determines both antigenic and host range specificity.

70-2386 NUCLEOTIDE POOL LEVELS IN GROWING, INHIBITED, AND TRANSFORMED CHICK FIBROBLAST CELLS. (E.) Colby, C. (U. California San Diego, La Jolla) and G. Edlin. Biochemistry (Wash.) 9(4):917-920, 1970.

Despite differences in growth kinetics at high and low initial cell densities, Rous sarcoma virus (RSV)-transformed chick embryo fibroblasts actively produced RSV. Measurements of nucleotide pool levels by labeling with $^{32}\text{PO}_4^{3-}$ showed that final levels of each ribonucleoside and deoxynucleoside triphosphate were similar when cultures were growing exponentially, were contact inhibited, or had been transformed by RSV. Thus, differences in nucleotide biosynthesis cannot account for differences in growth regulation exhibited by these cultures.

70-2387 MECHANISM OF ONCOGENIC TRANSFORMATION BY ROUS SARCOMA VIRUS. I. INTRA-CELLULAR INACTIVATION OF CELL-TRANSFORMING ABILITY OF ROUS SARCOMA VIRUS BY 5-BROMODEOXYURIDINE AND LIGHT. (E.) Balduzzi, P. (U. Rochester Sch. Med. Dent., N. Y.) and H. R. Morgan. J. Biol. Chem. 245(4):470-477, 1970.

Stationary phase chick embryo fibroblasts were infected with the Bryan strain of Rous sarcoma virus (RSV) and incubated with 5-bromo-2'-deoxyuridine (BUdR) for 18 hours, after which they were permitted to resume growth and synthesis of DNA in an enriched F12 medium containing serum and anti-RSV antibody. After 48 hours, cells were exposed to visible light and assayed for transformation foci. A 50-90% decrease in focus formation was seen; this phenomenon was not observed in cells exposed to BUdR for 18 hours before infection or on the day after infection, but only when cells were treated with BUdR at the time of infection. Cell death was not observed after treatment with BUdR and exposure to light in cultures in which almost all the cells were infected.

70-2388 RNA-DEPENDENT DNA POLYMERASE IN VIRIONS OF ROUS SARCOMA VIRUS. (E.) Temin, P. M. (U. Wisconsin McArdle Lab. Cancer Res., Madison) and S. Mizutani. Nature (London) 225(5252):1211-1213, 1970.

Evidence is presented which suggests that a polymerase is present in virions of Rous sarcoma virus (RSV) which catalyzes incorporation of deoxyribonucleotide triphosphates into DNA from an RNA template. DNA polymerase activity was found in concentrated RSV (Schmidt-Ruppin strain) purified by sucrose density gradient centrifugation and treated with a non-ionic detergent (Triton X-100) to disrupt virus and to observe full activity of the enzyme. If treatment was

carried out at 40° C, dithiothreitol had to be added to recover activity. Max. polymerase activity was found between 40-50° C and between pH 8-9.5. It is suggested that RNA in the virion may be masked by protein and that intact RNA is necessary for incorporation of thymidine triphosphate. Polymerase activity was not found in normal cell supernatant but was present in virions of avian myeloblastosis virus. No incorporation of ribonucleotide triphosphates was detected. These findings support the DNA provirus hypothesis and suggest that RNA tumor viruses have a DNA genome when they are in cells and an RNA genome when they are in virions.

70-2389 THE BIOCHEMICAL CHARACTERIZATION OF ALKALINE PHOSPHATASE FROM CHEMICAL- AND VIRAL-INDUCED THYMIC LYMPHOMAS OF C57BL MICE. (E.) Lumb, J. R. (Atlanta U., Ga.) and R. G. Doell. Cancer Res. 30(5):1391-1396, 1970.

Physical and chemical properties of alkaline phosphatase (APase) from thymic lymphomas of C57BL/Ka mice and of APase from the liver, spleen, duodenum and embryonic thymus of these mice were studied. Tumors were induced by urethan and 6-mercaptopurine (6-MP) (dose and route unspecified), by inj. of 7,12-dimethylbenzanthracene (75 µg in olive oil, s.c.) into neonatal mice, or by inj. of cell-free extracts of a 6-MP-induced lymphoma and further viral passage. APase activity was significantly lower in lymphomas induced by viruses than in those induced by chemicals. No correlation was found between APase activity and the latent period of the tumor or between the APase activity of virus-induced tumors and the number of viral passages. Derepression of APase may not be necessary for malignant transformation since both histochemical and biochemical data showed that a few of the tumors were negative for APase. No significant difference was found in the pH optimum of APase from tumors, embryo and spleen, but the pH optimum of APase from liver and duodenum was considerably lower. No significant difference in pH optimum among tumors induced by different agents was observed. Analysis of variance demonstrated that the heat inactivation constant of the liver enzyme was the only 1 significantly different from the others, but the biphasic shape of the curve for duodenal APase tended to differentiate it from both tumor and spleen enzymes. The ratio of APase activity toward β-glycerophosphate to that toward p-nitrophenyl phosphate showed the only significant difference was between liver and tumor APase. On acrylamide gel electrophoresis all APase preparations except the spleen extract gave 2 bands of activity, 1 of which contained the major portion of this activity.

70-2390 FELINE LEUKEMIA VIRUS DETECTION IN VITRO. (E.) Sarma, P. S. (NIH, Bethesda, Md.), R. J. Huebner, J. F. Baskar, L. Vernon, R. V. Gilden and R. Toni. Virology 41(2):377-381, 1970.

By means of electron microscopy, a newly developed complement fixation test for feline Type C viruses, and labeling of viral RNA with ^3H -uridine, feline leukemia virus (FeLV) was detected in feline embryonic fibroblast cultures grown in Eagle's minimum essential medium and inoc. with 10^4 - 10^6 infectious units of FeLV. Pleural fluid, a partially purified concentrate of a thoracic tumor, and 20% cell-free extracts of liver, tumor and spleen from 2 cats with lymphosarcoma were used as sources for the virus. Determinations were run 7, 13, 20 and 32 days after infection. Although tests for FeLV with these methods were positive as early as 7 days after infection and continued to be positive up to 32 days after infection, virus release into the culture medium was only detectable up to 2 weeks after infection with the labeling method despite the presence of extracellular and budding Type C particles in these infected cultures. Continued release of virus detectable by the ^3H -uridine method occurred only when cultures were serially transferred at 3-day instead of weekly intervals so that rapid viral growth was maintained.

- 70-2391 MORPHOLOGICAL STUDIES ON TRANSMISSIBLE FELINE FIBROSARCOMA. (E.) Snyder, S. P. (U. California Sch. Vet. Med., Davis), G. H. Theilen and W. P. C. Richards. Cancer Res. 30(6):1658-1667, 1970.

Fibrosarcomas were induced in 14/17 kittens by s.c. inj. of cell-free filtrates from S-T feline sarcoma virus into 1-6-day-old animals. Metastases, found in 7/17 cases, were of 2 different types, a solid tumor similar to those observed in s.c. tissue and another type, found primarily in the liver and brain, consisting of many cystic, blood-filled cavities surrounded by a thin shell of neoplastic cells (histologically similar to hemangiosarcomas). Electron and light microscopy revealed that all solid tumors consisted of fibroblasts, macrophage-like cells and mast cells. Typical Type C virions, with an outer diameter of about 115 m μ , were found budding from cytoplasmic membranes and into membrane-bound vacuoles within the cytoplasm of both fibroblasts and macrophage-like cells in the tumors of all inoc. kittens. Budding and immature particles were much more common than mature forms; intracisternal virus particles were also occasionally observed. These Type C particles were morphologically indistinguishable from those associated with feline leukemia.

- 70-2392 EXPERIMENTAL TRANSMISSION OF FELINE FIBROSARCOMA TO CATS AND DOGS. (E.) Gardner, M. B. (U. Southern California Sch. Med., Los Angeles), R. W. Rongey, P. Arnstein, J. D. Estes, P. Sarma, R. J. Huebner and C. G. Rickard. Nature (London) 226(5248):807-809, 1970.

Tumor tissue from a spontaneous s.c. fibrocarcinoma, caused by Type C feline sarcoma virus (FSV),

from a 5.5-yr.-old male Siamese cat was inj. through the uterine wall into 6 viable fetuses of a pregnant mixed-breed cat. After 22 days, 3 kittens were born; 2/3 developed tumors of the shoulder region when 45 and 71 days old, resp. The mother cat showed development of fibrosarcomatous nodules in the uterine wall and mesovarian ligament at necropsy 100 days after surgery. Cell-free virus extracts from kitten tumors or cat tumor homogenates induced sarcomas in 2-week-old puppies that had been inoc. in utero. Type C particles were found in tissues of most young animals with induced fibrosarcomas. Antisera from newborn dogs with FSV-induced fibrosarcomas were used to detect Type C RNA tumor virus antigens in complement fixation tests.

- 70-2393 MORPHOGENESIS OF BITTNER VIRUS. (E.) Gay, F. W. (Queen's U., Belfast, Ireland), J. K. Clarke and E. Dermott. J. Virol. 5(6):801-816, 1970.

Spontaneous mammary tumors from strain C3H mice were examined by electron microscopy for the morphogenesis of Bittner virus (mouse mammary tumor virus). Type A particles were seen forming near the nucleus and at the plasma membrane. Direct cell-to-cell transfer of virus was also seen occurring by pinocytosis of budding particles involving adjacent cells. It is suggested that features of the structure of internal components seen are related to the structure of mouse leukemia virus. Although intracisternal virus-like particles were sometimes seen in the tumor cells, the A particles are not thought to be related to Bittner virus.

- 70-2394 THE GROWTH ACCELERATING EFFECT OF BITTNER VIRUS IN MONOLAYERS OF BABY MOUSE KIDNEY CELLS. (E.) Links, J. (Netherlands Cancer Inst., Amsterdam) and O. Tol. J. Gen. Virol. 5(4):547-550, 1969.

Purified and partially purified Bittner virus (B particles) from mouse mammary tumors appeared to stimulate cell division in primary and secondary cultures of kidney cells from 5-day-old BALB/c DeA mice; purified virus also stimulated DNA synthesis. No morphological change or transformation was observed in these cultures or in BALB/c DeA mouse embryo cells prepared from 14-day-old embryos. It is not known which part of the Bittner virus stimulates DNA synthesis and mitosis.

- 70-2395 DISCOVERY OF VIRUS-LIKE PARTICLES IN CELLS OF TRANSPLANTABLE ADENOCARCINOMA 755. (Rus.) Proshchenko, V. G. (Inst. Exp. Clin. Oncol., Moscow). Vop. Onkol. 16(1):69-75, 1970.

Electron microscope study of ultrathin sections of mammary Adenocarcinoma 755 from 10 C57BL mice (6, 8, 9 and 10 days after transplantation of

the tumor) showed 2 types of virus-like particles, which correspond to Bernhard and Dalton's murine Type A and Type C virus, in the cells of the tumors. Type A particles found in the cytoplasm or in cytoplasmic vacuoles were considered to be either a variant of the milk factor or a precursor of Type B, or mature Bittner, virus. No Type B particles were found in the intercellular spaces of these adenocarcinomas, but it is possible that Type B particles were formed from Type A particles in the microvilli. The role of Type A particles, which were formed on membranes of the endoplasmic reticulum and located in its cisternae, is unknown. These particles were probably not involved in production of the tumor but were present as contaminants. Morphologically they were identical to virus particles which cause epizootics of diarrhea in newborn mice. Type C particles probably represent mouse leukemia virus, but further research is necessary to confirm this hypothesis.

70-2396 SEARCH FOR CROSS-REACTING ANTIGENICITY BETWEEN MAMMARY TUMOR VIRUS-INDUCED MAMMARY TUMORS AND EMBRYONIC ANTIGENS: EFFECT OF IMMUNIZATION ON DEVELOPMENT OF SPONTANEOUS MAMMARY TUMORS. (E.) Blair, P. B. (U. California Cancer Res. Genet. Lab., Berkeley). Cancer Res. 30(4):1199-1202, 1970.

Experiments performed on female BALB/cfC3H mice, infected with mammary tumor virus from allogenic (A/Crg1) or syngenic (BALB/cCrg1 and BALB/crC3HCrg1) issue, offered no evidence for the presence of embryonic antigens in mouse mammary tumors. Retreatment with embryonic extracts or tissue implants had little or no effect on tumor development in experimental animals. Mice were immunized with antigen from a spontaneous mammary tumor; with a mammary gland extract from a lactating female; and with tissue extracts and implants from embryos, newborns and adult mammary lands.

70-2397 BIOLOGICAL ACTIVITY OF VARIOUS ZONES OBTAINED BY ULTRACENTRIFUGATION OF THE MILK FACTOR OBTAINED FROM STRAIN PS MICE IN PREFORMED FICOLL GRADIENTS. (Fr.) Mouriquand, J. (Nuclear Study Ctr. Cell Biol. Lab., Grenoble, France), C. Mouriquand and C. Viala. Europ. J. Cancer 6(2):115-124, 1970.

When stored at -60°C and -195°C , cell-free extracts of mammary tumors from PS mice had the same biological activity when inj. i.p. into newborn C3H/eB, BALB/c and PS mice. However, extracts prepared by the Gross method lost their infectivity when stored at $+4^{\circ}\text{C}$ for 24-48 hours. Cell-free mammary tumor extracts prepared by Moore's method, defatted and deproteinized milk from PS mice, and mammary tumor cells grown in monolayer cultures, all gave 3 zones when subjected to ultracentrifugation in preformed ficoll gradients. Infectivity was spread over

the entire gradient, although virus particles were found only in zone 2 on electron micrographs. Some B particles were found in zones 2 and 3 obtained by ultracentrifugation of cell-free extracts from mammary tumors. Leukemia developed in 3/9 PS males at a mean age of 8.3 mo. and in 1/7 PS females at age 5.5 mo., after inoc. with extract prepared by Moore's method. Although activation of a latent virus might explain these findings in PS mice, it would not account for the development of leukemia in a 16-mo.-old female BALB/c mouse after inoc. with zone 3 obtained from ultracentrifugation of a cell-free extract of mammary tumor in Ficoll gradients. This case is probably due to transmission of a leukemogenic virus in the maternal milk.

70-2398 ISOPYCNIC ZONAL CENTRIFUGATION AND CHARACTERIZATION OF THE MOUSE MAMMARY TUMOR VIRUS (MTV) IN DIFFERENT GRADIENT SOLUTIONS. (E.) Manning, J. S. (U. California Cancer Res. Genet. Lab., Berkeley), A. J. Hackett, R. D. Cardiff, H. C. Mel and P. B. Blair. Virology 40(4):912-919, 1970.

Isopycnic zonal centrifugation and characterization of the mouse mammary tumor virus (MTV), taken from MTV-infected milk, in different gradient solutions revealed increased UV absorbance and MTV B-particle antigenicity. The isodensities of MTV were comparable to those of other RNA tumor viruses. Two distinct light-scattering bands were formed by centrifugation of MTV-positive preparations in preformed sucrose- or K tartrate-containing gradients. Only those bands at the higher buoyant density contained characteristic MTV particles; the bands of lower isodensity consisted of virus-like particles of varying size and shape (possibly incomplete MTV particles). MTV-free milk samples did not show light-scattering bands nor virus-like particles.

70-2399 MAMMARY TUMOR VIRUS ASSOCIATED ANTIGENS ON THE MEMBRANE OF INFECTED MOUSE SPLEEN CELLS. (E.) Daams, J. H. (Netherlands Cancer Inst., Amsterdam), J. Calafat, E. Y. Lasfargues, B. Kramarsky and P. Bentvelzen. Virology 41(1):184-186, 1970.

Tissue cultures were initiated from the spleens of 6-week-old C57BL and BALB/c mice infected with mammary tumor virus (MTV) by foster nursing on RIII milk. All cell suspensions from cultures at the time of transfer showed the presence of an MTV antigen at the cell membrane and in the cytoplasm. MTV membrane antigen was confirmed in BALB/cfRIII spleen cells after 16 weeks and in C57BLfRIII spleen cultures after 20 weeks. It is concluded that the MTV genome must be maintained in spleen cells. The MTV genome is unable to cause production of complete viral particles but seems to control antigen production at the cell surface.

70-2400 BIOCHEMICAL CONSEQUENCES OF TYPE 2 ADENOVIRUS AND SIMIAN VIRUS 40 DOUBLE INFECTIONS OF AFRICAN GREEN MONKEY KIDNEY CELLS. (E.) Friedman, M. P. (Jefferson Hosp. Med. Coll., Philadelphia, Pa.), M. J. Lyons and H. S. Ginsberg. J. Virol. 5(5):586-597, 1970.

African green monkey kidney (AGMK) cells are restrictive hosts for Type 2 adenovirus (Ad) even though a small number of virions can be formed. Except with low virus multiplicities, Ad infected almost all of the cells, and almost all cells synthesized virus-specific early proteins and DNA. The major restriction is synthesis of capsid proteins, but a few cells do synthesize these. When AGMK cells were infected with both SV40 and Ad, about 50% of the cells synthesized Ad capsid proteins. About the same quantity of Ad DNA was synthesized in restricted and in SV40-enhanced infections. In mixed infections, however, synthesis of host DNA was not stimulated as in cells infected only with SV40 and replication of SV40-DNA was inhibited, the degree of inhibition being dependent upon the multiplicity of Ad employed. Addition of 50 µg/ml of cycloheximide prevented SV50-induced enhancement of Ad multiplication while addition of 5×10^{-6} M 5-fluoro-2-deoxyuridine had no effect on enhancement. It is suggested that SV40 induces the synthesis of a protein necessary for propagation of Ad, that the protein is not a constituent of the cells, and that the protein cannot be produced by Ad.

70-2401 CROSS-REACTING TUMOR-SPECIFIC TRANSPLANTATION OF ANTIGENS IN TUMORS INDUCED BY ADENOVIRUSES 3, 14, AND 12. (E.) Ankerst, J. (U. Lund, Sweden) and H. O. Sjögren. Cancer Res. 30(5):1499-1505, 1970.

From the results of a study of immunosensitivity in vitro and immunogenicity in vivo in mouse strains A/Sn and CBA and (A/Sn x CBA)F₁ and (A/Sn x C57B1)F₁ hybrids it is concluded that tumors induced by adenovirus (Ad) Types 3, 7, 12 and 14 share a common tumor-specific transplantation antigen. The ⁵¹Cr release method showed that sera from mice immunized against syngenic Ad-12 tumors were cytotoxic to hamster Ad-7 and Ad-14 tumor cells but not to BHK-C13 control cells. In colony inhibition tests made on hamster Ad-3 and Ad-14 tumor cells, the lymph node cells of similarly immunized mice exhibited specific cytotoxicity. Treatment of mice with hamster Ad-14 tumor cells induced an immunity against Ad-12 tumor cells. This was demonstrated by isograft immunity and as a cytotoxic activity in vitro of serum and lymph node cells derived from treated mice. Treatment of mice with hamster Ad-3 tumor cells also induced immunity to Ad-12 tumor cells. This was detected in vitro as a cytotoxic effect of lymph node cells from treated mice and a weak isograft resistance to Ad-12 tumor cells. The reason for this weaker immunity is not known, but it may be that the

isograft immunity test is less sensitive than the colony inhibition test. Alternatively, the effect of the sensitized lymphocytes may be blocked in vivo by humoral antibodies which, for some reason, might be induced in larger quantities by Ad-3 than by Ad-14 tumor cells.

70-2402 INDUCTION OF T ANTIGEN, NEW SURFACE ANTIGEN, AND TRANSPLANTATION IMMUNITY BY A NONTUMORIGENIC VARIANT OF TYPE 3 BOVINE ADENOVIRUS. (E.) Nishibe, Y. (Kyoto U. Inst. Virus Res., Japan), Y. Nakamura and Y. K. Inoue. Cancer Res. 30(6):1795-1798, 1970.

A nontumorigenic variant (WB-PS) of Type 3 bovine adenovirus, which had previously been isolated from wild type virus in stable porcine kidney (PS) cells, induced T antigen and a new cell surface antigen in PS cells. T antigen was detected with the direct fluorescent antibody (FA) test and surface antigen by the indirect FA test. When inj. s.c. at birth with the WB-PS variant, hamsters became immune to transplantation of tumor cells transformed by the wild type strain of type 3 bovine adenovirus.

70-2403 CLONAL ANALYSIS OF TUMORIGENESIS OF BOVINE ADENOVIRUS TYPE 3 AND ISOLATION OF A NONTUMORIGENIC VARIANT. (E.) Nishibe, Y. (Kyoto U. Inst. Virus Res., Japan), T. Kimura and Y. K. Inoue. Arch. Ges. Virusforsch. 29(2-3):195-204, 1970.

From a study of the tumorigenicity of the wild type strain, 3 isolated clones (BA, BB, BC), and an experimentally induced variant (WB-PS), it is concluded that bovine adenovirus Type 3 is a heterogeneous population of virus particles with different tumorigenic potentialities. When inj. s.c. into newborn hamsters, the wild type strain produced nonprogressive solid or cystic tumors, after a latent period of 4-8 weeks. Clones BA, BB and BC induced tumors which were progressive in about 50% of all cases; none of the hamsters inj. with these clones developed cystic tumors even when inoc. with more than 10^5 TCD₅₀. Virus-neutralizing antibodies were found in titers of 1:20-1:128 in sera from hamsters with nonprogressive tumors produced by the wild type strain; these antibodies were found in only a few sera from hamsters with tumors induced by clone BA. The WB-PS variant, which produced a cytopathic effect in primary calf kidney cells but not in stable porcine kidney cell cultures, produced no tumors when inj. s.c. in hamsters. This variant was specifically neutralized by anti-clone BA or BB immune sera of Type 3 bovine adenovirus, but not by anti-Type 1 bovine adenovirus immune serum. However, anti WB-PS variant immune serum failed to neutralize clone BA virus. The lack of reciprocal cross-neutralization with antiserum to WB-PS variant may be interpreted as a loss or change in the specificity of 1 or more antigen components of WB-PS variant.

0-2404 INVESTIGATION ON INTRANUCLEAR PARACRYSTALLINE INCLUSIONS INDUCED BY ADENOVIRUS 5 IN KB CELLS. (E.) Boulanger, P. A. (INSERM Unit Res. Biochem. Proteins, Lille, France), G. Torpier and G. Blsert. J. Gen. Virol. 6(2):329-332, 1970.

Intranuclear paracrystalline inclusions, induced in KB cells after infection with adenovirus Type 5, were extracted from the cells and examined under the electron microscope. Structures similar to the virus DNA-nucleoid, partially attached nucleoids and completely encapsidated virus particles were observed in close association with the paracrystal. It is suggested that these inclusions are a reserve of structural proteins for the biosynthesis of the virus nucleoid; this is supported by the fact that only structural proteins of adenovirus were found in sucrose and Cernulol extracts of the paracrystal. Anti-fluorescent antiserum to adenovirus Type 5 showed large fluorescent polyhedral intranuclear inclusions corresponding to paracrystals.

2405 PARADOXICAL EFFECT OF FREUND'S COMPLETE ADJUVANT UPON TRANSPLANTATION EFFICIENCY OF ADENOVIRUS-INDUCED TUMOUR CELLS. (E.) Alford, C. (George Washington U. Sch. Med., Washington, D.C.) A. Hollinshead and R. J. Huebner. J. Gen. Virol. 5(4):541-543, 1969.

Though Freund's complete adjuvant (FCA) usually enhances tumor immunity, pretreatment with FCA apparently enhanced tumor formation in hamsters challenged with adenovirus Type 12 tumor cells. Inbred, 3-4-week-old female Syrian golden hamsters were inj. i.p. with 0.2 ml FCA 17 days before s.c. challenge with adenovirus Type 12 transformed hamster cells in Eagle's minimum essential medium. All FCA-treated animals developed tumors after inj. of 10^4 , 10^5 , and 10^6 cells. Of the hamsters receiving no adjuvant, 1/3 of those inoc. with 10^4 cells and 1/2 with 10^5 cells developed tumors; all of those inoc. with 10^6 cells developed tumors.

2406 STUDY OF ADENOVIRUS TYPE 12 BEHAVIOR IN MONKEYS. (Rus.) Adzhigitov, F. I. (Inst. Exp. Path. Ther., Sukhumi, USSR), Iu. S. Gubeladze, D. A. Gubeladze and B. A. Sanguliia. Virus 15(1):105-109, 1970.

In contrast to other laboratory animals, 17 young rhesus monkeys, 7 *Papio hamadryas*, and 10 rhesus monkeys, all less than 1 yr. old) did not develop any tumors or hematopoietic changes after i.p. and s.c. inj. of large doses of adenovirus Type 12 (Ad-12). During an observation period of more than 2 yr., 10 of the monkeys survived and 7 others died of unrelated causes. The complement-fixation (CF) test, performed on all 17 animals 1 mo. after infection, showed that 13 had CF antibodies to Ad-12 in titers of 1:10-1:80; these titers

later decreased, indicating that the virus does not persist in monkeys. In addition, 4 animals had CF antibodies to antigen from tumors induced in hamsters with Ad-12. These antibodies are apparently formed as a response to T antigen which is produced soon after infection by the action of adenovirus on sensitive cells. The absence of antibodies to T antigen, which was observed at later periods, might serve as an objective test for the absence of transformed neoplastic cells which synthesize T antigen.

70-2407 STUDIES OF TUMOR ANTIGENS IN HAMSTER TUMORS INDUCED BY ADENOVIRUS TYPE 12. (Ger.) Erb, P. (U. Basel Inst. Microbiol. Hyg., Switzerland). Path. Microbiol. (Basel) 34(2):112-127, 1969.

Tumors were induced in newborn hamsters by s.c. inoc. of a suspension of Huie strain adenovirus Type 12. They were then transplanted into 2-8-day-old hamsters by s.c. inoc., where they were permitted to grow for an additional 6-8 weeks, prior to isolation and partial purification of 3 antigen components of different sizes (which immunodiffusion studies proved to be serologically identical). Further gel chromatography reduced the number of components to 2, possibly due to an association of some antigen particles with foreign protein. The smaller of the 2 was heat-stable and specific for adenovirus Types 12, 18 and 31; the larger was heat-labile and specific for adenovirus type 12, alone. Further study of this larger component showed that it consisted of 3 serologically identical, heat-labile sub-components; the 2 smaller components became heat-stable following additional gel chromatography.

70-2408 APPLICATION OF THE PAIRED RADIOIODINE-LABELED ANTIBODY TECHNIQUE (PRILAT) TO THE DETECTION OF ADENOVIRUS 12 TUMOR (T) ANTIGEN. (E.) Evans, M. J. (Roswell Park Mem. Inst., Buffalo, N. Y.) and D. S. Yohn. J. Immunol. 104(5):1132-1142, 1970.

The paired radioiodine-labeled antibody method (PRILAT) was 10-fold more effective than immunofluorescence and 100-200-fold more effective than complement fixation in detection of adenovirus-12(Ad-12) T-antigen in Ad-12-infected HEp2 cells and in Ad-12 hamster tumor cells. This method allowed for direct calculation of μg quantities of immune- and nonimmune-labeled globulins. In synchronously infected HEp2 cells, PRILAT was capable of detecting *de novo* synthesis of Ad-12 T antigen 8 hours after infection. Release of P antigen from infecting virions 4 hours after infection was considered responsible for a specific evanescent reaction. The conc. of T-antigen was max. 36 hours after infection.

70-2409 TRANSPLANTATION OF ADENOVIRUS TYPE 12-INFECTED NEWBORN HAMSTER TISSUE INTO YOUNG ADULT HAMSTERS. DETERMINATION OF PERIOD FOR CARCINOGENESIS OF TARGET CELLS. (Jap.) Fujita, H. (Okayama U. Med. Sch., Japan). J. Karyopath. 12(3):125-132, 1969.

Admin. of adenovirus Type 12 (Ad12) to newborn hamsters was followed by s.c. transplantation of peritoneal tissues to 16-29-day-old hamsters. Tumors developed when tissues were transplanted 6 or more hours after virus inoc. Inj. of Ad12 (i.p.) to other newborn hamsters, followed by similar transplantation methods, gave results comparable to tumor development (within 24-38 days) in newborn hamsters directly inj. with virus. Controls, 10 young hamsters, inoc. with Ad12 showed no tumor development after 46-367 days. It is concluded that 6 hours after i.p. inj. of virus in newborn hamsters, irreversible changes in target cells occurred.

70-2410 TRANSFORMATION BY ADENOVIRUS TYPE 12 OF KIDNEY CELL CULTURES FROM A NEWBORN GREEN MONKEY. (Rus.) Adzhigitov, F. I. (Inst. Exp. Path. Ther., Sukhumi, USSR) and Iu. S. Krivoshein. Vop. Virus. 15(2):221-225, 1970.

Kidney cell cultures from a 1-day-old green monkey were inoc. with human adenovirus Type 12 (Ad-12). Within 5-6 days after inoc., the specific cytopathic effect (CPE) of Ad-12 became evident and cell degeneration reached a max. during the next 2 weeks. The medium was still changed, but each time 50% of the old medium was retained. After 30-40 days new cells began to grow in most of the cultures that had exhibited the CPE, and after 2.5 mo. solid monolayers were formed. In a period of more than 2 yr., 50 passages were made and 8 cell lines with different properties were established. Lines 1-4 consisted primarily of fibroblast-like cells while lines 5-8 were, for the most part, epithelioid cells with a small number of spindle cells. Some of these cell lines still contained Ad-12 as was demonstrated by production of its specific CPE in HeLa cells and by the production of 2 undifferentiated sarcomas at the site of inj. within 5 and 6 mo. after s.c. inj. of 6 newborn hamsters with cell suspensions. These 2 hamsters who developed tumors had serum antibodies to tumor antigen. Even after an observation period of 2 yrs, no neoplasm formed when cells from line 3 were inj. into the testicular parenchyma of a male green monkey which had been treated with cortisone acetate. Transformation of the kidney cell cultures by Ad-12 might have occurred by transformation of the remaining cells after sensitive cells had been destroyed or by selection of resistant cells, followed by their gradual transformation. It is suggested that Ad-12 persisting in the cell cultures is a mutant of the original virus.

70-2411 A COMPARISON OF ADENOVIRUS 12 INDUCED T AND TUMOUR ANTIGENS BY RATE-ZONAL CENTRIFUGATION. (E.) Potter, C. W. (U. Sheffield, England), J. S. Oxford and B. C. McLaughlin. J. Gen. Virol. 6(1):105-116, 1970.

Rate-zonal centrifugation in linear sucrose gradients of antigen extracts from human embryonic kidney (HEK) and human carcinoma (HEp-2) cells infected with adenovirus 12 (Ad-12) revealed 2 species or molecular forms of T antigen. These T antigens had molecular wt. estimated at $8-9 \times 10^4$ and $4-5 \times 10^4$ daltons and were distinct from Ad-12 hexon and fiber antigens, with estimated molecular wt. of $22-25 \times 10^4$ and $6-7 \times 10^4$ daltons, resp. Results were identical whether Ad-12 antigens were extracted from HEp-2 or HEK cells. By the same method, 2 species of tumor antigen were found in extracts from transplanted Ad-12 tumors in CBA mice and hamsters, and from the H212 and TAD111 lines of Ad-12-induced hamster tumor cell lines. The molecular wt. of these tumor antigens were similar to the molecular wt. of the T antigens. Differences were found, however, in the relative proportions of the 2 species of antigen in tumor extracts and in T antigen extracts. Thus, tumor antigens and T antigens cannot be assumed to be identical. Sedimentation behavior of tumor antigens was not altered by treatment with RNase or sodium deoxycholate. These findings suggest that the tumor antigens are not necessarily bound to RNA and that the antigen with the larger molecular wt. is not an aggregate form of the antigen with the smaller molecular wt. It is also possible, however, that tumor antigen may be resistant to RNase treatment and the larger antigen may be an aggregate which is not split by sodium deoxycholate.

70-2412 COMPARATIVE SUSCEPTIBILITY OF NON-INBRED AND STRAIN LSH INBRED SYRIAN HAMSTERS TO THE ONCOGENIC ADENOVIRUSES. (E.) Van Hoosier, G. L., Jr. (Washington State U., Pullman), J. G. Burke and J. J. Trentin. Proc. Soc. Exp. Biol. Med. 134(2):427-429, 1970.

Newborn, noninbred and strain LSH inbred Syrian hamsters were inoc. s.c. or i.p. with human adenovirus type 12 (AV-12) or simian adenovirus (SA-7) and observed for tumor formation. There was no apparent sex difference for either group and the i.p. route was more effective for tumor production. Noninbred hamsters were more susceptible to Av-12 than the LSH strain; and for SA-7, tumors developed in 91% and 94%, resp.

70-2413 INDUCTION OF SPECIFIC TUMOR IMMUNITY IN HAMSTERS WITH GREEN MONKEY ADENOVIRUS SA7(C8). (Rus.) Babakova, S. V. (P. A. Gertsen Sci. Res. Inst. Oncol., Moscow), N. N. Dodonova, E. M. Tsetlin, V. V. Gorodilova,

I. Ageenko and A. D. Al'tshteln. Vop. Onkol. (3):40-46, 1970.

rian hamsters, aged 2-3 mo., were rendered immune to the development of SA7 tumors by s.c. inj. of a 7 virus suspension (0.5 ml) obtained from tumors induced in newborn hamsters by s.c. inj. of SA7 virus; this tumor immunity was specific. Cross-immunity to SA7 tumors was not observed when hamsters were inj. with SV20, SV38, SV40 or human adenovirus Type 2. Tumor immunity was induced by the original SA7 virus and by its large and small plaque-forming variants. The minimum dose required to produce immunity was more than 10^5 LD₅₀ which is 100-fold higher than the minimum oncogenic dose of this virus. Immunity induced by SA7 virus developed 3-7 days after inj. and reached a max. after 14-20 days. Tumor growth was increased if the immunizing virus was inj. 24 hours before tumor cell transplantation; the mechanism involved in this phenomenon is unknown. Transplantation antigen was present in only some of the primary tumors studied. Two metastases from tumors which did contain transplantation antigen grew well in both normal and immune hamsters.

2414 PATHOGENESIS OF ONCOGENIC SIMIAN ADENOVIRUSES: VIII. THE HISTOPATHOLOGY AND ULTRASTRUCTURE OF SIMIAN ADENOVIRUS 7-INDUCED INTRACRANIAL NEOPLASMS. (E.) Merkow, L. P. (Allegheny Gen. Hosp. Singer Mem. Res. Inst., Pa.), M. Slifkin, M. Pardo and N. P. Rapoza. Exp. Rec. Path. 12(3):264-274, 1970.

born, noninbred Syrian hamsters were inoculated with simian adenovirus Type 7 (SA-7; inj. into right cerebral hemisphere) and tumor development was observed by fluorescence and electron microscopy. Cells of the intracranial (IC) neoplasms were then cultured *in vitro* and some were superinfected with SA-7. IC neoplasms developed in 392/422 (93%) hamsters in 27-88 days; 30% of the tumor-developing animals showed paralysis followed by paralysis. Neoplasms involved the choroid plexus, cranial nerve V, mater and calvarium. Virus-like particles were noted in cells of SA-7-induced IC neoplasms cultured *in vitro*. Neoplastic cells contained VLP in the cytoplasm *in vivo*. VLP similar to replicating SA-7 particles seen in the nucleus of superinfected cells cultured *in vitro*. SA-7 T antigen was seen as the focus of nuclear fluorescence in 100% of the cells; cells did not show fluorescence.

2415 DEMONSTRATION OF A TUMOUR AND TRANSPLANTATION ANTIGEN IN HAMSTER TUMOURS INDUCED BY AN AVIAN ADENOVIRUS (CELO). (E.) G. C. (Nat. Inst. Med. Res., London), J. Oxford and C. W. Potter. Arch. Ges. Viroforsch. 29(1):25-31, 1970.

Antigen-specific tumor antigen was found in a cell culture line derived from a chick embryo

lethal orphan (CELO) virus-induced hamster tumor, as shown by tumor transplant immunity and immunofluorescence. Results were similar for both the Petak and Phelps strains of CELO.

70-2416 ON THE ONCOGENIC PROPERTIES OF CHICKEN EMBRYO LETHAL ORPHAN VIRUS, AN AVIAN ADENOVIRUS. (E.) Jones, R. F. (U. Texas Southwestern Med. Sch., Dallas), B. B. Asch and D. S. Yohn. Cancer Res. 30(6):1580-1585, 1970.

Two groups of newborn golden Syrian hamsters administered s.c. inj. of chicken embryo lethal orphan virus (CELO; $10^{9.3}$ or $10^{9.0}$ LD₅₀) showed tumor development in 7/13 (54%) and 8/99 (8%), resp. Only 1 of an additional group of 26 hamsters administered virus (inactivated from $10^{8.7}$ to $10^{4.0}$ LD₅₀) developed a tumor. Tumor latent period was 14-52 weeks and 13/16 of the tumors occurred in females. A total of 15/16 tumors appeared at the site of virus inj.; 12/16 were sarcomas. Both indirect immunofluorescence and complement fixation tests failed to show antibody in the sera of tumor-bearing hamsters to autologous tumor extracts or to CELO-infected chick and hamster embryo cells.

70-2417 PATHOGENESIS OF ONCOGENIC SIMIAN ADENOVIRUSES. VII. THE ORIGIN OF ANNULATE LAMELLAE IN LLC-MK2 CELLS INFECTED WITH SV30. (E.) Merkow, L. P. (Allegheny Gen. Hosp. Singer Mem. Res. Inst., Pittsburgh, Pa.), M. Slifkin, M. Pardo and N. P. Rapoza. J. Ultrastruct. Res. 30(3-4):344-353, 1970.

Monolayers of LLC-MK2 monkey kidney cells were studied 1-192 hours after infection with simian adenovirus 30 (SV30). Intracellular annulate lamellae were seen within 1 hour after infection and seemed to be formed by a sequential delamination of individual lamellae on both sides of the nuclear envelope. Parallel lamellae were connected by tubular structures. Ribosome-like electron-dense particles and crystalloid bodies in contact with the lamellae were also seen.

70-2418 SUPPRESSION OF ANTIBODY FORMATION AGAINST SENDAI VIRUS IN THE SV40 AND ADENOVIRUS 16 INFECTED HAMSTERS. (E.) Hamburg, V. P. (Inst. Exp. Clin. Oncol., Moscow), O. E. Scherbakova and G. J. Svet-Moldavsky. Experientia 26(5):532-534, 1970.

Male, 2-mo.-old Syrian hamsters were inoculated i.p. with SV40 or human adenovirus Type 16 (Ad-16) and were inoculated 9 days later with active Sendai virus (0.5 ml, i.p.). Previous inoculation with SV40 or Ad-16 suppressed formation of antibodies against Sendai virus. Simultaneous injection of SV40 and Sendai virus resulted in no immunosuppression. It is suggested that the inhibition of an immunological response brought about by these 2 different DNA viruses is necessary for carcinogenesis and malignant growth.

70-2419 VARIANTS OF DEFECTIVE SIMIAN PAPOVAVIRUS 40 (PARA) CHARACTERIZED BY CYTOPLASMIC LOCALIZATION OF SIMIAN PAPOVAVIRUS 40 TUMOR ANTIGEN. (E.) Butel, J. S. (Baylor U. Coll. Med., Houston, Tex.), M. J. Guentzel and F. Rapp. J. Virol. 4(5):632-641, 1969.

Synthesis of SV40 tumor (T) antigen was induced in the cytoplasm of green monkey kidney (GMK) cells by 3/112 isolates of a hybrid consisting of particles aiding replication of adenovirus (PARA)-adenovirus 7 (AV7). These clonal progeny were derived by 2 successive plaque purifications in GMK cells. The 3 isolates were identified as PARA-AV7 populations by several methods. Synthesis of cytoplasmic T antigen by these variants and of intranuclear T antigen by parental PARA-AV7 and complete SV40 were not inhibited by arabinofuranosylcytosine (10 µg/ml) but were inhibited by cycloheximide (25 µg/ml). Pools of sera which reacted with intranuclear SV40 T antigen also reacted with the cytoplasmic antigen induced by the variant viruses. Cytoplasmic antigen was identified as serologically similar or identical with intranuclear SV40 T antigen by adsorption experiments. Since the variant viruses produced cytoplasmic SV40 T antigen in monkey, rabbit and human cells, the species of the host cell apparently played no role in the localization of this antigen. It is suggested that these 3 viral variants lack some virus-mediated transport mechanism, which shifts the T antigen from the cytoplasm to the nucleus.

70-2420 DENSITY DIFFERENCES BETWEEN HYBRID AND NONHYBRID PARTICLES IN TWO ADENOVIRUS-SIMIAN VIRUS 40 HYBRID POPULATIONS. (E.) Baum, S. G. (Albert Einstein Coll. Med., Bronx, N. Y.), W. H. Wiese and W. P. Rowe. J. Virol. 5(3):353-357, 1970.

The E46⁺ strain of adenovirus 7, which is a hybrid genome of adenovirus 7 and SV40 DNA in an adenovirus 7 capsid, and adenovirus 2+t⁷, a hybrid genome of adenovirus 7 and SV40 DNA in an adenovirus 2 capsid, were subjected to fixed-angle equilibrium density gradient centrifugation in cesium chloride. Both hybrids, which are always contaminated with nonhybrid adenovirus, separated into 2 bands. The band with the lower buoyant density was enriched in hybrid particles, particularly in the case of adenovirus 2+t⁷, but density differences were not great enough to permit preparative separation of hybrid from nonhybrid populations. As with deletion mutants of λ bacteriophage, the lower density of hybrid virions, which have gained an extra DNA fragment, may be explained by a more than compensatory loss of adenovirus DNA. This is consistent with the defectiveness of the hybrid as an adenovirus.

70-2421 VARIATION IN PROPERTIES OF PLAQUE PROGENY OF PARA (DEFECTIVE SIMIAN PAPOVAVIRUS 40)-ADENOVIRUS 7. (E.) Rapp, F.

(Pennsylvania State U. Coll. Med., Hershey), S. Pauluzzi and J. S. Butel. J. Virol. 4(5):626-631, 1969.

By means of 2 successive plaque purifications in green monkey kidney cells, 112 clonal lines were derived from a hybrid defective SV40 (PARA)-adenovirus 7 population. Of these 112 lines, 92 (82%) produced 234 tumors in 1393 newborn hamsters; these positive clones produced tumors in 4-55% of the inoc. animals, depending upon the clone. There was no relationship between PARA titer and tumorigenicity or between PARA titer and the latent period of the tumors. Analysis of the tumor (T) antigen content of tumors showed that 171/219 contained only SV40 T antigen and 48/219 tumors contained T antigens for both SV40 and adenovirus; the antibody response of the host corresponded perfectly with the T antigen content of the tumors. All 12 tumors which first became palpable 6-10 weeks after inoc. contained both SV40 and adenovirus T antigens, but the adenovirus T antigen was found in less than 10% of tumors which appeared 16 or more weeks after inoc. No virus clones were derived which induced mixed tumors exclusively; tumors developed in other animals which contained only SV40 T antigen. Therefore it is suggested that some mechanism must operate in the hamster cells to suppress the expression of the adenovirus genes in some instances.

70-2422 QUANTITATIVE CHARACTERISTICS OF THE TRANSFORMATION OF HAMSTER CELLS BY PARA (DEFECTIVE SIMIAN VIRUS 40)-ADENOVIRUS 7. (E.) Duff, R. (Pennsylvania State U. Milton S. Hershey Med. Ctr., Hershey) and F. Rapp. J. Virol. 5(5):568-577, 1970.

A fluorescent-focus assay was developed for quantitative measurement of transformation induced in hamster embryo fibroblasts by a hybrid of defective SV40 and adenovirus 7 (Ad-7). Transformation by hybrid particles followed one-hit kinetics with a ratio of 1 FFU:250 PFU. The total number of foci which developed depended upon the method used to adsorb virus, but quantitative results remained the same no matter what method was used. The transforming efficiency of the hybrid virus is far greater than that of the parental SV40 or Ad-7. This suggests selection of a highly oncogenic variant, elimination of a transformation inhibitor in the portion of the genome lost from the defective virus, or synergism between defective Ad-7 and SV40 genomes found in the hybrid. Since all transformed foci contained SV40 T antigen but none contained only Ad-7 T antigen, nearly all transformation events were at least partially dependent upon the SV40 part of the viral genome. Single foci induced by the hybrid virus were isolated and grown into cell lines. These consisted of cuboidal cells with a SV40-type morphology or epithelial cells with an Ad-type morphology. Both types contained SV40 T and S

tigens but only the epithelial cells contained -7 T antigen. Tumors were produced in weanling Syrian hamsters inj. with 5/5 cell lines. Antibodies to both SV40 and Ad-7 were found in hamsters with tumors.

2423 IN VITRO TRANSFORMATION BY ADENOVIRUS-SIMIAN VIRUS 40 HYBRID VIRUSES. IV. PROPERTIES OF CLONES ISOLATED FROM CELL LINES TRANSFORMED BY ADENOVIRUS 2-SIMIAN VIRUS 40 AND ADENOVIRUS 12-SIMIAN VIRUS 40 TRANSCAPSIDANT HYBRID VIRUSES. (E.) Black, P. H. (Harvard Med. Sch., Boston, Mass.), L. D. Berman and C. B. Brown. J. Virol. 4(5):694-703, 1969.

Evidence is presented to show that the wide range of findings reported for adenovirus-SV40 transcapisidant hybrids can be explained by multiple events occurring during transformation and carcinogenesis. Clones were isolated from weanling Syrian kidney cells transformed with adenovirus 12-SV40 (ad 2+t⁷) and adenovirus 12-SV40 (ad 12+t⁷) hybrids. Most cultures exhibited one of 3 different types of cellular and colonial morphologies: (1) those characteristic of adenovirus (Ad)-transformed cells, (2) those characteristic of SV40-transformed cells, and (3) those with an intermediate or mixed morphology which included features of both SV40- and Ad-transformed cells. Although calcium concentration affects the morphology of Ad-transformed cells, it had no effect on these hybrid-transformed cells. Cells with an SV40 or intermediate morphology contained SV40 T antigen. Cell lines derived from ad 12+t⁷ hybrid virus transformations which had an intermediate morphology contained Ad 12 T antigen as well, while cells with a typical Ad morphology contained only Ad 12 T antigen. Ad 7 and Ad 2 T antigens were not detected with the sera. Clones with an SV40 morphology produced tumors predominantly with an SV40 histology while clones with an Ad morphology produced typical Ad tumors. Clones with an intermediate morphology produced tumors with an intermediate histology.

24 IN VITRO TRANSFORMATION BY THE ADENOVIRUS-SIMIAN VIRUS 40 HYBRID VIRUSES. I. VIRUS-SPECIFIC RIBONUCLEIC ACID IN CELL LINES TRANSFORMED BY THE ADENOVIRUS 2-SIMIAN VIRUS 40 AND ADENOVIRUS 12-SIMIAN VIRUS 40 TRANSCAPSIDANT HYBRID VIRUSES. (E.) Levin, M. J. (NIH, Bethesda, Md.), P. H. Black, S. L. Coghill, C. B. Brown and P. H. Henry. J. Virol. 4(5):704-711,

the results of RNA-DNA hybridization experiments with adenovirus 2-SV40 (ad 2+t⁷) and adenovirus 12-SV40 (ad 12+t⁷) transcapisidant hybrids it is concluded: (1) at least 3 different events occur during transformation of weanling Syrian kidney cells by the hybrid virus population; (2) the morphology of the resulting clones

is determined by the viral genome or genomes present; (3) the linkage of adenovirus (Ad) 7-SV40 genomes is confirmed since these genomes were never found to be dissociated; (4) defective Ad 7-SV40 genomes are capable of causing transformation; and (5) the transcapisidant particle is probably composed of only Ad 7 and SV40 genetic information. A correlation was found between the results of RNA-DNA hybridization and the morphology of transformed cells and colonies. The Ad 7 and SV40 genomes were present in transformed cells which had an SV40 morphology while only adenovirus genetic information was found in cells with a typical Ad morphology. Cells with intermediate morphologies contained Ad 7 and SV40 genomes; those transformed with ad 2+t⁷ also had Ad 2 genomes and those transformed with ad 12+t⁷ also had Ad 12 genomes.

70-2425 ISOLATION OF TWO PLAQUE VARIANTS FROM THE ADENOVIRUS TYPE 2-SIMIAN VIRUS 40 HYBRID POPULATION WHICH DIFFER IN THEIR EFFICIENCY IN YIELDING SIMIAN VIRUS 40. (E.) Lewis, A. M., Jr. (Nat. Inst. Allerg. Infect. Dis., Bethesda, Md.) and W. P. Rowe. J. Virol. 5(4):413-420, 1970.

Two genetically stable variants were isolated from the hybrid Ad++ population, a monkey cell-adapted line of the Ind. 2 strain of adenovirus Type 2 (Ad-2). These plaque variants, which were both hybrids of Ad-2 and SV40, differed in the efficiency with which they yielded SV40. SV40 virions recovered from both the high-efficiency yielder (HEY) and low-efficiency yielder (LEY) grew to a high titer in African green monkey kidney (AGMK) cells, were of the minute plaque type, and were fully susceptible to SV40-neutralizing antibodies. The parent, HEY, and LEY populations all formed Ad plaques in human embryonic kidney (HEK) cells with 1-hit kinetics and formed Ad plaques in AGMK cells by 2-hit kinetics. When HEY and LEY populations were plaqued on lawns of non-hybrid Ad, the number of plaques increased and the kinetics of plaque induction were converted to 1-hit. SV40 plaque induction by the parent and HEY populations followed 1-hit kinetics. Because of interference with the assay by the Ad virus cytopathic effect at the low dilutions employed and because of the small number of SV40 plaques induced by the LEY population, the kinetics of SV40 plaque induction could not be determined with this variant. Both the HEY and LEY variants produced detectable SV40 T antigen in 10-70% of HEK cells, but only the HEY variant induced SV40 V antigen in 1-10% of the cells. These findings suggest that with the LEY variant SV40 V antigen formation appears to be blocked. It is postulated that the differences in SV40-yielding efficiency between these variants are due to the recombinant DNA composing the genome of the hybrid particles.

70-2426 EQUILIBRIUM DENSITY GRADIENT STUDIES ON SIMIAN VIRUS 40-YIELDING VARIANTS

OF THE ADENOVIRUS TYPE 2-SIMIAN VIRUS 40 HYBRID POPULATION. (E.) Wiese, W. H. (Nat. Inst. Allerg. Infect. Dis., Bethesda, Md.), A. M. Lewis, Jr. and W. P. Rowe. J. Virol. 5(4): 421-426, 1970.

High-efficiency SV40-yielding (HEY) variant of a hybrid adenovirus Type 2-SV40 population was partially purified from nonhybrid adenovirus 2 (Ad-2) by fixed-angle equilibrium density gradient centrifugation in cesium chloride. This population consists of nonhybrid Ad-2 virions, small quantities of nonhybrid SV40 virions, and Ad-encapsidated particles containing infectious SV40 genome. Hybrid virions of the HEY variant and SV40 yielding particles banded at densities 0.004 g/ml lighter than nonhybrid Ad-2 virions. In 2 cycles of centrifugation, 100-fold purification of the hybrid was obtained. Findings also suggest that another class of hybrid virion, which is slightly more dense than nonhybrid Ad-2 virions, is present in the HEY population. No evidence of purification was found when the low-efficiency yielding (LEY) variant of this hybrid was subjected to the same kind of centrifugation. The difference in buoyant density between the LEY hybrid particles and the major component of the HEY hybrid particles was surprising and suggests that the LEY genome contains a much larger piece of Ad DNA than the HEY genome. It is also possible that this difference is related to the markedly less efficient production of SV40 by the LEY variant.

70-2427 REQUIREMENT FOR CELL REPLICATION AFTER SV40 INFECTION FOR A STRUCTURAL CHANGE OF THE CELL SURFACE MEMBRANE. (E.) Ben-Bassat, H. (Weizmann Inst. Sci., Rehovot, Israel), M. Inbar and L. Sachs. Virology 40(4):854-859, 1970.

SV40-induced structural changes in the surface membrane of 3T3 cells were measured by agglutination with the carbohydrate-binding protein concanavalin A. It was demonstrated that cell replication was necessary for these surface membrane changes to occur and for the loss of this change to occur in abortively-transformed cells. Agglutination with concanavalin A occurred only in multiplying cultures and required at least 1 cell generation and a density of about 10^5 cells/cm². The percentage of cells containing T antigen in multiplying cultures was of the same order of magnitude as the 50% of cells that formed aggregates 6 days after SV40 infection and was much higher than the 1% that made up transformed colonies. About 90% of the agglutinated cells contained T antigen. It is indicated that abortive transformation can produce the same surface membrane changes as hereditary transformation.

70-2428 IMMUNE RESPONSE OF RABBITS TO PURIFIED PAPOVAVIRUS SV40. (E.) Tevethia, S. S. (Baylor U. Coll. Med., Houston, Tex.). J. Immun. 104(1):72-78, 1970.

New Zealand White rabbits synthesized antibodies to both the non-virion T antigen and to viral (V) antigen when inoc. i.v. with a single large dose of purified SV40 (2×10^{11} - 1×10^{12} virus particles) while rabbits inoc. i.v. with a small dose (1×10^9 virus particles) synthesized antibodies to V antigen only. Restimulation of these rabbits by another small dose of virus inoc. i.v. on day 28 failed to induce synthesis of T antibody. Rabbits inoc. with both large and small doses of SV40 developed virus-neutralizing antibodies. Sucrose density gradient centrifugation showed that antibody activity against the T antigen was associated with 19S and 7S immunoglobulins.

70-2429 BLOCKING EFFECT OF HUMAN ADENOVIRUS TYPE 16 ON THE DEVELOPMENT OF TUMORS INDUCED WITH PAPOVA VIRUS SV40. (Rus.) Gamburg, V. P. (Inst. Exp. Clin. Oncol., Moscow), L. P. Trubcheninova and O. E. Shcherbakova. Vop. Virus. 15(1):112-113, 1970.

Oncogenic activity of SV40 was significantly reduced when newborn, noninbred Syrian hamsters were inj. simultaneously with SV40 and human adenovirus Type 16 (Ad-16) which had been passaged 6-8 times in HeLa cells and then in human embryonic kidney cells. Strain A426 of SV40 was mixed with adenovirus (10^7 TCID₅₀/0.2 ml) and inj. s.c. into hamsters; 61 controls received s.c. inj. of SV40 only. Tumors developed in 12/43 (30%) experimental animals and in 53/61 (87%) controls. Tumors developed after 98 and 113 days in the control and experimental animals, resp. Suppression of tumor development was not seen when Ad-16 was grown on HeLa cells and its cytopathic effect was lower. The most likely explanation for tumor suppression is that Ad-16 interferes with the oncogenic activity of SV40, but it is also possible that the blocking effect might be due to an unknown human virus present in the culture fluid used to grow human embryonic kidney cells. Replication of Ad-16 might activate replication of this unknown virus.

70-2430 STUDY OF THE TRANSFORMING ACTIVITY OF SV40 VIRUS IN CELL CULTURES. (Rus.) Sarycheva, O. F. (Control Inst. Med. Biol. Preps., Moscow), A. D. Al'tshtein and N. N. Dodonova. Vop. Virus. 14(6):727-734, 1969.

Only embryonic guinea pig kidney cells did not undergo transformation when monolayer cultures of kidney cells from golden hamsters, mice (lines C57Bl, C3HA, CC57Br) and embryonic guinea pigs and embryonic skin-muscle cells from hamsters, mice and rats (August and Wistar strains) were inoc. with a variety of SV40 strains which produce large and small plaques. In the kidney cell cultures, transformed cells were large and epithelioid while in the embryonic skin-muscle cell cultures they were fibroblast-like spindle or polygonal cells. An immunofluorescence study of 33 lines of serially passaged transformed

ster and mouse kidney cells and embryonic se, rat and hamster skin-muscle cells showed t almost 100% of the cells contained SV40 or antigen. When hamster kidney cells or ryonc hamster skin-muscle cells were incubated h strain A-426 of SV40 virus for 1 week, cell nsformation was more evident at 40° C than at C. Large-plaque forming strains A-426 and were only 2-67% as active in producing cell nsformation in hamster kidney cells as small- que forming strain 128. The minimum dose of ain 128 which produced cell transformation e less than 1/100 of that of the other 2 ins.

431 PREVENTION OF TUMOR GROWTH BY IMMUNIZA-
TION OF HAMSTERS WITH X-IRRADIATED
-TRANSFORMED CELLS. (Heb.) Ashkenazi, A.
Klan Hosp., Rehovoth, Israel) and Z. Zadik.
fuah 77(9):376-379, 1969.

g hamster kidney cells transformed by SV40 s, 3 sublines were derived according to ction of tumors from animals with or without stases. Fluorescent antibody and complement tion tests showed that the original plus its blines contained equal amounts of SV40 tumor gen. Tumors grew faster and gave rise to stases earlier and in more animals for 2 of (sublines; the third subline produced tumors e grew at an intermediate rate. Morphological nination of the original and subline HK7T1 ed different patterns of growth with the is of the original line tending to grow close cher and having an epithelial appearance, ared to a spreading and fibroblastic appear- in the subline. These differences remained gh several passages. The HK7T1 line had a broader spectrum and stronger transplantation en and gave better protection in animals ized with X-irradiated HK7T1 cells than the al line. The value of these lines for u of tumor growth and invasiveness is sted.

32 SV40 VIRUS-INDUCED TUMOUR SPECIFIC
TRANSPLANTATION ANTIGEN IN CULTURED
CELLS. (E.) Smith, R. W. (NCI, Bethesda,
J. Morganroth and P. T. Mora. Nature
(London) 227(5254):141-145, 1970.

ro assay methods were developed for SV40- ad tumor-specific transplantation antigen i with SV40-transformed kidney cells from aice (SV-AL/N), SV40-transformed 3T3 cells BALB/c mice (SV-BALB/3T3), and SV40-trans- 3T3 cells from noninbred Swiss mice (SV- and syngenic AL/N, BALB/c, and Swiss mice. 3 cell lines absorbed out c ototoxic ty when they were incubated with sera from ized mice, indicating that the transplanta- antigen was tumor-specific. Incubation of cells from mice inj. with polyoma-trans- AL/N kidney cells (PY-AL/N) or SV-AL/N

cells specifically killed PY-AL/N and SV-AL/N target cells, resp. Target cell death also resulted from incubation of spleen cells from irradiated animals inj. with SV-AL/N cells and from non-irradiated animals sensitized to crude membrane from SV-AL/N cells. Results from spleen cell assays correlated well with those from the serum assay, but spleen cell assays demonstrated activity that would otherwise be missed. It was demonstrated that TSTA is stable and immunogenic in mouse cell membranes. SV-AL/N crude membrane induced both serum and spleen cell mediated toxicity, as demonstrated in vitro. By means of cellular fractionation and the serum assay method, SV40 TSTA was seen on the cell surface, microsomes and mitochondria of SV-AL/N cells, but not in the nuclear or soluble cyto- plasmic fractions.

70-2433 DEVELOPMENT OF TUMORS FROM CELLS WHICH
HAVE BEEN TRANSFORMED IN VITRO BY SV40
VIRUS. (Rus.) Al'tshtein, A. D. (L. A. Tarasevich
State Control Inst. Med. Biol. Preps., Moscow),
E. M. Tsetlin, N. N. Dodonova, O. F. Sarycheva,
I. S. Levenbuk and A. E. Chigirinskii. Vop.
Onkol. 16(1):63-69, 1970.

No tumors were produced in isologous animals when 3-5 x 10⁶ cells of embryonic rat and mouse fibroblasts, which had been transformed by SV40, were inj. s.c. into 3-5-day-old animals. This was not attributed to an inability of these cells to multiply in vivo, since they produced tumors within 1 week at the site of inj. when inj. into cheek pouches of hamsters; these tumors regressed completely in the next 3-4 weeks. Embryonic mouse fibroblasts which had not been transformed did not produce tumors in hamsters. This inability of transformed mouse and rat fibroblasts to produce tumors in isologous animals is attributed to the formation of a new, virus-inducing transplantation antigen on the surface of these cells. Transformed embryonic hamster fibroblasts produced "epithelioid cell" sarcomas and transformed embryonic hamster kidney cells produced carcinosarcomas and adeno- carcinomas when inj. s.c. into 2-3-mo.-old Syrian hamsters. These tumors were readily cultivated in vitro and retained their tumori- genicity for hamsters. Tumors grown in vitro were morphologically identical to those grown in vivo except for marked differences in the distribution of T antigen in the nuclei. The ability of transformed hamster cells to induce tumors in isologous animals may be related to the high susceptibility of Syrian hamsters to the tumorigenic effect of SV40 virus.

70-2434 IDENTIFICATION OF THE SIMIAN VIRUS 40
WHICH REPLICATES WHEN SIMIAN VIRUS 40-
TRANSFORMED HUMAN CELLS ARE FUSED WITH SIMIAN
VIRUS 40-TRANSFORMED MOUSE CELLS OR SUPERINFECTED
WITH SIMIAN VIRUS 40 DEOXYRIBONUCLEIC ACID.
(E.) Kit, S. (Baylor Coll. Med., Houston, Tex.),

T. Kurimura, M. Brown and D. R. Dubbs. *J. Virol.* 6(1):69-77, 1970.

SV40 was rescued by fusion of SV40-transformed mouse kidney cells with SV40-transformed cells from human skin or from clonal lines of cells from the human buccal mucosa. By fusing transformed human cells with mouse cells transformed by SV40 plaque morphology mutants, it was demonstrated that the rescued SV40 originated in transformed mouse cells. Either the SV40 genome in transformed human cells was not activated or defective particles were produced which were not detected by plaque assay on African green monkey kidney (CV-1) cells. When transformed human cells were superinfected with plaque morphology mutants of SV40-DNA, only replication of the superinfecting DNA was observed. The SV40 genome in transformed human cells may have been released from integration in cells superinfected with SV40, but either replication was minimal or the particles produced were noninfectious for CV-1 cells.

70-2435 INITIAL SITE OF SYNTHESIS OF VIRUS DURING RESCUE OF SIMIAN VIRUS 40 FROM HETEROKARYONS OF SIMIAN VIRUS 40-TRANSFORMED AND SUSCEPTIBLE CELLS. (E.) Wever, G. H. (Baylor Coll. Med., Houston, Tex.), S. Kit and D. R. Dubbs. *J. Virol.* 5(5):578-585, 1970.

SV40 was rescued from SV40-transformed hamster (TSV-5) cells by fusion with susceptible African green monkey kidney (CV-1) cells in the presence of UV-irradiated Sendai virus. The sites in which SV40 is produced during rescue were determined by isolating nuclei from fused cells at various times after fusion, separating them on sucrose-density gradients, and assaying for infectious center formation and virus content on CV-1 monolayers. At 40 hours after fusion, virus was first detected in transformed nuclei; at 68-72 hours virus was associated with both transformed and susceptible nuclei. The ratio of CV-1 and TSV-5 nuclei containing virus at this time corresponds to the initial cell fusion ratio (2:1), suggesting that all nuclei in a heterokaryon produce virus. Thus, viral rescue apparently does not depend upon transfer of SV40-DNA to a susceptible CV-1 nucleus since the transformed nucleus is the primary site of virus production. The time sequence of events in the rescue process corresponds with that occurring during productive infection.

70-2436 STIMULATION OF CELL GROWTH IN VITRO BY SERUM WITH AND WITHOUT GROWTH FACTOR. RELATION TO CONTACT INHIBITION AND VIRAL TRANSFORMATION. (E.) Jainchill, J. L. (Columbia-Presbyterian Med. Ctr., New York, N. Y.) and G. J. Todaro. *Exp. Cell Res.* 59(1):137-146, 1970.

Comparisons were made of the growth rates of sparse and confluent cultures of 3T3 and BALB/3T3

mouse cell lines; SV40-transformed cells derived from 3T3 and BALB/3T3 which had lost contact inhibition of cell division; Sv-F1-101, a variant derived from a cloned line of SV40-transformed 3T3 which had a relatively low saturation density; and BALB/3T3 cells transformed by murine sarcoma virus (MSV) which had lost contact inhibition. In general, cell lines with a low saturation density were unable to grow in a medium deficient in serum growth factor (sgf) while transformed cells grew well under these conditions. The exception was SV-F1-101 in which low saturation density appeared to be dissociated from a high requirement for sgf. Although SV-F1-101 required little sgf, it maintained a low cell density despite a high division rate. The low cell density was apparently the result of an equilibrium between proliferation and detachment. BALB/3T3 cells transformed by MSV which had lost contact inhibition were able to grow on medium deficient in sgf while "revertant" subclones which were contact inhibited, and no longer shed MSV, were not. Murine leukemia virus can chronically infect BALB/3T3 but, unlike MSV, it did not change either the saturation density or ability to grow in growth-deficient medium. The continued presence of SV40 and MSV genetic material in the cells was apparently associated with a pronounced decrease in the requirement for sgf.

70-2437 DEOXYRIBONUCLEIC ACID REPLICATION IN SIMIAN VIRUS 40-INFECTED CELLS. III. COMPARISON OF SIMIAN VIRUS 40 LYTIC INFECTION IN THREE DIFFERENT MONKEY KIDNEY CELL LINES. (E.) Ritzi, E. (Princeton U., N. J.) and A. J. Levine. *J. Virol.* 5(6):686-692, 1970.

Studies of the kinetics of SV40 lytic infection of 3 monkey cell lines (African green monkey kidney (AGMK), BSC-1 and CV-1) showed viral DNA synthesis and increased viral infection beginning between 20-24 hours after infection in the AGMK and CV-1 cultures, compared to 36-45 hours after infection in the BSC-1 culture. The 1-step growth curve for infectious SV40 production was similar for CV-1 and AGMK cells. SV40 induction of cellular DNA synthesis was seen for the CV-1 and AGMK cells, but not for BSC-1 cells. Fragmentation of high-molecular wt. cellular DNA to low molecular wt. forms after SV40 infection was seen mainly for AGMK cells; after 96 hours, 13-32% of the DNA had decreased molecular wt., as compared to about 2% of the CV-1 or little or none of the BSC-1 cellular DNA. It is concluded that different responses are due to involvement of cell functions in the virus-induced cellular DNA synthesis mechanism.

70-2438 SUSCEPTIBILITY TO SUPERINFECTION OF SIMIAN CELLS TRANSFORMED BY SV40. (E.) Rapp, F. (Pennsylvania State U. Coll. Med., Hershey) and S. C. Trulock. *Virology* 40(4): 961-970, 1970.

African green monkey kidney cells (BSC-1) transformed by SV40 were tested for susceptibility to reinfection by the homologous virus and found to synthesize the SV40-specific tumor antigen, the surface antigen and the transplantation rejection antigen. Fusion of the transformed cells with cells susceptible to SV40 replication failed to show infectious SV40. Human adenovirus (V) types 2, 7 and 12 replicated in the cells but not in the parental nontransformed cells), indicating that either the part of the SV40 genome which aids HAV replication in simian cells is present in the transformed cells, or that an adenovirus (AV)-sensitive cell population was selected. SV40 failed to replicate in the transformed cells, while simian AV 7, and Types 1 and 2 herpes viruses replicated in both parental and transformed cells. Use of a defective SV40 genome encapsidated in an AV coat (PARA particle) resulted in replication of PARA particles, indicating that a defective genome can be replicated in a SV40-transformed cell.

439 DNA REPLICATION IN SV40 INFECTED CELLS. I. ANALYSIS OF REPLICATING SV40 DNA. Levine, A. J. (Princeton U., N. J.), H. S. and F. E. Billheimer. *J. Molec. Biol.* 54:549-568, 1970.

A study of SV40 replication in African green monkey kidney cells, ^3H -labeled thymidine was incorporated into viral DNA about 15 hours after infection. The rate of viral DNA synthesis reached a max. at 30 hours and decreased thereafter. Infectious virus first appeared 24 hours after infection and its conc. continued to increase for at least 72 hours. Sedimentation of viral DNA through neutral sucrose gradients demonstrated that little or no supercoiled viral DNA (20-21S) was synthesized during the first 5 hours of labeling with ^3H -thymidine (30 hours after infection). Instead, the viral DNA form was present sedimented at 24-25S. Column chromatography on benzoylated-naphthoylated acrylaminoethyl-cellulose was used to fractionate mature (21S) and replicating (25S) DNA. Viral supercoiled DNA was eluted with 0.6 M sodium chloride soln. while replicating DNA remained bound to the column, to be eluted later with caffeine. Electron micrographs of viral DNA obtained from the caffeine-eluted fraction of the column showed that replicating molecules have 2 branch points, 3 branches and visible ends. About 75% of these molecules completed 90-95% of their replication. It is concluded that there is a slow or rate-limiting step late in the replication process. This slow step might be due to low levels of viral or host cell recombination enzymes.

20 FIVE YEARS OF OBSERVATION OF MONKEYS INFECTED WITH SV40 IN THE FIRST FEW MONTHS AFTER BIRTH. (Rus.) Talash, M. (Sci. Res. Inst. Polio Viral Encephalitis, Moscow),

M. P. Chumakov and T. I. Zavodova. *Vop. Virus.* 14(3):301-305, 1969.

SV40 virus (strain A-426) was inj. into 4 *Papio hamadryas* and 1 green monkey, i.m. (3×10^8 PFU) and intracerebrally (0.5×10^8 PFU). Inj. were given to 3 *P. hamadryas* and to the green monkey 1 day after birth. The remaining *P. hamadryas* was inj. at age 3 weeks. The 5 mothers of these infected monkeys, which remained in close contact with their offspring, served as controls. All of the infected monkeys and controls remained asymptomatic and none developed tumors during the 5-yr. observation period. Virus was excreted with the feces and was present in the blood of infected monkeys from 3-7 weeks after infection. Virus-neutralizing antibodies were observed for the 5-yr. after infection. Natural infection with SV40 probably developed in 1 of the infected monkeys, since the titer of virus-neutralizing antibodies in this case was higher 5 yr. after infection than 1 yr. after infection. Virus was also isolated from the blood of the controls who had elevated titers for virus-neutralizing antibodies. This confirms that SV40 is highly contagious in monkeys. Although these findings indicate that SV40 is not oncogenic for monkeys, it may be that the 5-yr. observation period is not long enough for tumor development.

70-2441 EARLY EVENTS IN THE INFECTION OF PERMISSIVE CELLS WITH SIMIAN VIRUS 40: ADSORPTION, PENETRATION, AND UNCOATING. (E.) Barbanti-Brodano, G. (Wistar Inst. Anat. Biol., Philadelphia, Pa.), P. Swetly and H. Koprowski. *J. Virol.* 6(1):78-86, 1970.

African green monkey kidney cells were infected with ^3H -leucine- or ^3H -thymidine-labeled SV40 and in 2 hours the peak (50%) of thymidine-labeled virus had been adsorbed. By 30 min., most cytoplasmic radioactivity was associated with large granules and the nuclei were also appreciably labeled. Nuclei contained more ^3H -leucine than ^3H -thymidine. Intact virions were found in the nuclei from 0.5-2.5 hours after infection; uncoating of intranuclear virions occurred from 2.5-4.0 hours after infection; this was followed by breaks of the circular DNA structure of the viral genome and the appearance of a new component (sedimenting at 76S), possibly of viral origin. It is suggested that parental viral coat proteins in the nucleus are involved in the regulation of the transcription and replication of viral DNA.

70-2442 MORPHOLOGICAL ASPECTS OF THE UPTAKE OF SIMIAN VIRUS 40 BY PERMISSIVE CELLS. (E.) Hummeler, K. (Child. Hosp. Philadelphia, Pa.), N. Tomassini and F. Sokol. *J. Virol.* 6(1):87-93, 1970.

Cultures of African green monkey kidney cells were infected with SV40 and studied by electron

microscopy for changes after 10-45 min. and 1-48 hours. After 10 min., virus particles were seen attached to the cell membrane, with virus uptake occurring by 2 mechanisms: 1) engulfment of single particles and 2) pinocytosis involving several particles/vesicle. By 1 hour, nuclear and acquired cell membranes had fused as the particles passed into the nucleus, allowing the original virus to alter nuclear morphology. Uncoating of nuclear viral particles was completed by 4 hours, when they were no longer discernible. Morphological evidence of viral replication was seen 24 hours after infection.

70-2443 ELECTRON MICROSCOPIC STUDIES OF THE DEVELOPMENT OF SV40 IN KIDNEY CELLS OF *Erythrocebus patas*. (Ger.) Hecker, W. (U. Basel Inst. Microbiol. Hyg., Switzerland) and H. Löffler. *Path. Microbiol.* (Basel) 33(6):350-360, 1969.

Primary kidney-cell cultures of *E. patas*, infected with a suspension of SV40 virus, were examined by electron microscopy at intervals of 2-336 hours post infection (p.i.). Phagocytized viral particles disappeared from view, with only a few being followed to the vicinity of the nuclear membrane. These also disappeared prior to observable decapsidation or penetration into the nucleus. Viral particles were not seen in the nucleus until 36-48 hours p.i., although the nucleus was almost filled with them at 3 or 4 days, when they showed arrangement in thickly-packed, crystalline groups. Two forms were clearly discernible with different densities and inner structures. As these passed back into the cytoplasm, beginning on day 5, they showed a high degree of affinity for the surfaces of plasma organelles and the swollen membranes of the endoplasmic reticulum. Some particles were also released into the culture medium by an "exocytic process," prior to lysis of the host cells on days 10-14 p.i.

70-2444 ELECTRON MICROSCOPIC STUDY OF KIDNEY CELLS OF *Erythrocebus patas* INFECTED WITH SV40. (Ger.) Hecker, W. (U. Basel Inst. Microbiol. Hyg., Switzerland). *Path. Microbiol.* (Basel) 34(3-4):134-135, 1969.

Three to 4 days after infection, numerous SV40 virus particles were demonstrable in the nuclei of cultures of kidney cells of *E. patas*. These consisted of poorly delimited, contrast-rich viruses and less dense particles with a small nucleoid, which were surrounded by a double membrane. From day 5 on, the viruses migrated through the nuclear pores into the cytoplasm, showing an affinity for the surfaces of plasma organelles, with free viruses and virus-containing vacuoles also attaching themselves to the membrane of the endoplasmic reticulum and the inner surface of the cell membrane. Mature particles then began to escape from the cell by means of an "inverse" phagocytosis, in which the membrane

surrounding individual particles or groups of virus particles became slowly evaginated and separated from the rest of the membrane. When the cells became lysed, 10-14 days after infection, both unattached viruses and those which had adsorbed to membrane surfaces were set free into the culture medium.

70-2445 ELECTRON MICROSCOPIC STUDIES OF KIDNEY CELLS OF *Erythrocebus patas* AFTER INFECTION WITH SV40 AND ADENOVIRUS TYPE 12. (Ger.) Hecker, W. (U. Basel Inst. Microbiol. Hyg., Switzerland). *Arch. Ges. Virusforsch.* 29(2-3):222-240, 1970.

The helper effect of SV40 on the replication of adenovirus Type 12 (Ad-12) in kidney cells of *E. patas* cultured *in vitro* was max. when infection with SV40 preceded infection with Ad-12 by 48 hours. When such double infections were studied at intervals of 12-144 hours after the second infection, irregular bundles of long fibers, consisting of early protein and Ad-12 T antigen, appeared in the nucleus between hours 12-16. Between hours 16-48, the appearance of 4 different types of inclusion bodies masked the much slower replication of SV40 entirely, while far-reaching changes of the structure of the nucleolus, similar to those reported in Ad-12-infected cultures of KB cells, indicated the active participation of this body in viral synthesis. Other changes in the nucleus, during subsequent stages of infection, were identical to those seen in *E. patas* kidney cells infected with Ad-12 alone and in a number of established lines of human tumor cells following similar infection. It is concluded that the helper effect of SV40 was limited to stimulation of Ad-12 replication, in terms of both speed and quantity, in the absence of any significant qualitative influence.

70-2446 THE INTERACTION OF SV40 WITH SV40-TRANSFORMED AND NON-TRANSFORMED MONKEY KIDNEY CELLS. (E.) Sauer, G. (Inst. Virus Res., Heidelberg, Germany) and E. C. Hahn. *Z. Krebsforsch.* 74(1):40-47, 1970.

A comparison was made of the interaction of SV40 with SV40-transformed African green monkey kidney (GMK) cells, which are resistant to productive SV40 infection, and the infection of permissive CV-1 cells. As shown by incubation with SV40 labeled with ³H-thymidine, the virus adsorbed readily to both cell types but not more than 10-20% of the radioactivity became permanently associated with the cells. This suggests that the adsorbed virus could have been eluted and inactivated, a suggestion which is supported by the finding that some radioactivity, which was initially attached to the cells, returned later to the supernatant. Uncoating, defined as the appearance of acid-insoluble, DNase-susceptible radioactivity,

occurred in only 4-5% of the virus in transformed cells and in as much as 20% in the CV-1 cells. When SV40-transformed GMK cells were superinfected with SV40, viral infectivity decreased rapidly in the medium and cells. The titers of extracted infectious DNA also decreased, but to a lesser extent than viral infectivity. This persistent infectious DNA could be cell-associated virus which has lost its infectivity.

2447 DEOXYRIBONUCLEIC ACID REPLICATION IN SIMIAN VIRUS 40-INFECTED CELLS. II. DETECTION AND CHARACTERIZATION OF SIMIAN VIRUS PSEUDOVIRIONS. (E.) Levine, A. J. (Princeton N. J.) and A. K. Teresky. J. Virol. 5(4): 457, 1970.

Purified SV40 virions grown in primary African green monkey kidney (AGMK) cells contained cellular DNA. Labeled DNA was found in the virions of a large-plaque mutant of SV40 virus grown in primary AGMK cells labeled with ^3H -thymidine 4 days before inoc. This DNA is most likely in the virion since it is resistant to DNase, sediments at 250S, and can be precipitated with antiserum to purified SV40 virions. When virions were lysed with 0.6% cationic dodecyl sulfate, the ^3H -labeled fraction sedimented at 14S. In a DNA-DNA hybridization experiment this fraction had a base sequence more like cellular DNA than viral DNA. Sedimentation through neutral and alkaline sucrose gradients revealed that this 14S DNA is composed of DNA molecules of different sizes that sediment between 11 and 15S. Because of this heterogeneity in size, SV40 virions containing cellular DNA (pseudovirions) have a variable DNA: capsid protein ratio and exhibit a spectrum of densities in CsCl equilibrium gradients. Little or no cellular DNA was found in purified preparations of wild-type SV40 virus grown in BSC-1 or CV-1 cells.

2448 SURFACE ANTIGEN(S) OF SV40-TRANSFORMED TUMOR CELLS. (E.) Häyry, P. (Wistar Inst. Anat. Biol., Philadelphia, Pa.) and V. Virology 41(1):22-29, 1970.

Immunological (mixed hemagglutination (MHA), direct immunofluorescence (IF)) analysis of surface antigens of SV40-transformed tumor cells (hamster lines, 3 mouse lines) gives evidence suggesting that these antigens are components of the normal cell surface, exposed by a virus-specific uncovering mechanism. Spontaneously or SV40 virus-transformed cell lines and non-transformed lines were converted from a MHA or nonreactive state to a reactive state as a result of mild proteolytic enzyme treatment. Antigens thus exposed were found to cross-react with the SV40-transformed cell surface antigens regardless of the species origin of the cells. It seems unlikely that the antigenic specificity is determined by hematoside or

H-acetylglucosamine or that it crossreacts with Forssman antigens.

70-2449 THE EVOLUTION OF SV40 VIRUS ANTIGEN IN MONKEY KIDNEY CELL CULTURES (R 1 CA). QUALITATIVE AND QUANTITATIVE IMMUNOFLOUORESCENT STUDY. (E.) Sapatino, V. (St. S. Nicolau Inst. Inframicrobiol., Bucharest), I. Aderca and M. Iftimovici. Rev. Roum. Inframicrobiol. 6(4): 307-313, 1969.

Qualitative and quantitative immunofluorescent study of the SV40 virus antigen in monkey kidney cell cultures (R 1 CA) revealed the assembly of the virus in the capsid. Synthesis of the SV40 virus in a nuclear ribonucleoprotein network is suggested.

70-2450 INDUCTION OF TUMOR-ANTIGEN FROM SV40 VIRUS IN VARIOUS TISSUE CULTURES. (Rus.) Al'tshtein, A. D. (L. A. Tarasevich State Control Inst. Med. Biol. Preps., Moscow) and O. F. Sarycheva. Vop. Virus. 15(1):78-84, 1970.

The A426 strain of SV40 virus, which forms large plaques, produced specific tumor (T) antigen in the nuclei of monolayer cultures from the kidneys of green and rhesus monkeys, hamsters and embryonic guinea pigs and from embryos of humans, hamsters, C3Hf mice and Wistar rats. The percentage of cells containing T antigen reached a maximum within 48-96 hours after inoc. and remained at about the same level for 1-10 days. The percentage of cells containing T antigen was highest in green and rhesus monkey kidney cells and in human embryonic cells; these were the only cultures in which SV40 virus had a cytopathic effect (CPE). This suggests that in only some of the rodent cells in which T antigen forms is there a complete cycle of virus maturation. The resistance of some cell culture to the CPE of SV40 virus was not due to the inability of the virus to adsorb on the cells or to interferon formation. With an immunofluorescence method, a linear relationship was established between the dose of SV40 virus and the percentage of green monkey kidney cells containing T antigen 48 hours after inoc. Because of its accuracy and specificity this method can be used for quantitative detection of small amounts of SV40 virus. The rate of T antigen formation increases when the temperature is raised from 37° C to 40° C and decreases when the temperature is lowered to 32° C.

70-2451 FURTHER STUDIES ON THE DIFFERENCES IN THE INTERACTION OF SIMIAN VIRUS 40 WITH AFRICAN GREEN MONKEY KIDNEY AND HUMAN DIPLOID CELLS. (E.) Carp, R. I. (Wistar Inst. Anat. Biol., Philadelphia, Pa.) and F. Sokol. J. Gen. Virol. 5(3):433-436, 1969.

Efficiency of infection with SV40 viral DNA and the net synthesis of RNA hybridizable with purified SV40 DNA in human diploid (WI-38) and African green monkey kidney (GMK) cells infected with SV40 were determined. The ratio of the efficiency of induction of T antigen-positive cells in GMK cells to that in WI-38 cells was similar, whether whole virus or infectious DNA was used as the infectious agent. This supports the previous finding that the early aspects of the cell-virus relationship, such as adsorption and entrance into eclipse, are not responsible for the differences in the 2 cell systems. The differences appear to be related to events occurring after stripping of the DNA and resultant possible transcription. The amount of hybridizable RNA in WI-38 cells was the same as that found in cultures of GMK cells with a comparable number of T antigen-positive cells, but was much less than that found in GMK cells infected with a high multiplicity. These findings suggest a possible block in the transcription process in the majority of WI-38 cells. Or, translation of an early function may be blocked; this could be expressed as a reduction in the synthesis of virus-specific RNA. A further possibility is that virus-specific RNA is more rapidly destroyed in WI-38 than in GMK cells and is not accumulated even though extensive transcription occurs.

70-2452 PROPERTIES OF SIMIAN VIRUS 40 RESCUED FROM CELL LINES TRANSFORMED BY ULTRA-VIOLET-IRRADIATED SIMIAN VIRUS 40. (E.) Kit, S. (Baylor U. Coll. Med., Houston, Tex.), T. Kurimura and D. R. Dubbs. J. Virol. 4(5):585-595, 1969.

By fusion with susceptible green monkey kidney (CV-1) cells, SV40 strains were rescued from 35/83 clonal lines of mouse kidney cells that had been transformed by UV-irradiated SV40. Failure to rescue SV40 from clones which produced little virus was not due to failure to fuse with CV-1 cells, but to low input multiplicities. All but 4 of the rescued SV40 strains had properties of the parental SV40 in CV-1 cells: they induced transplantation antigen, intranuclear SV40 T-antigen, thymidine kinase, DNA polymerase, and cellular DNA synthesis and formed infectious virus with kinetics similar to parental SV40 at either 37° C or 41° C. The 4 mutants, which were obtained from clones, which were "poor" yielders, replicated at 37° C but very poorly at 41° C. However, all other SV40 strains rescued from "poor" and "rare" yielders resembled parental SV40. This could be explained if the integrated viral genome were normal, if the transformed cell had properties which interfere with SV40 rescue or if the integrated viral genome were defective.

70-2453 VIRUS PRODUCTION IN CULTURES OF SIMIAN VIRUS 40-TRANSFORMED HUMAN AMNION CELLS. (E.) Fogh, J. (Sloan-Kettering Inst. Cancer Res., New York; N. Y.), J. Loveless and

E. Gaffney. J. Nat. Cancer Inst. 45(1):149-162, 1970.

SV40-infected and -transformed primary cultures of human amnion epithelial cells (HAE) synthesized SV40 at all stages of infection before and during "crisis." The 3-phase pattern of SV40 production (1, high production; 2, low yields; 3, increased yields prior to "crisis"), attributed to a series of shifts in the balance between the amount of available SV40 and the susceptibility of the transformed cells to reinfection, was not dependent on input multiplicity or the age of the cultures at the time of infection. However, the time at which phase 3 occurred depended upon input multiplicity and transfer dilution factors. Large numbers of virus-producing cells (infectious centers or V antigen-containing cells) were seen shortly after SV40 infection in HAE cultures. In contrast to infected fibroblast cultures, however, this phase in HAE cultures was not followed by an increase in virus-producing cells to involve nearly the entire population. Before the "crisis" phase, virus-producing cells increased significantly in HAE cultures (in contrast to a decrease in fibroblast cultures). The frequency of inclusion body-containing cells in HAE cultures was correlated with SV40 titers in the supernatant. At culture transfer, the morphology and growth patterns of the transformed cells varied according to the phase of SV40 production, which in turn was inversely related to cell recovery. "Crisis" was correlated with a cellular change towards reduced SV40 resistance. Since SV40 superinfection did not induce premature "crisis," it is concluded that the "crisis" phase requires a certain number of cell divisions.

70-2454 INCREASED RESISTANCE OF SV40 TRANSFORMED HUMAN AMNION CELLS TO POLIOVIRUS INFECTION. (E.) Hahn, E. (German Cancer Ctr. Inst. Virus Res., Heidelberg) and J. Fogh. Arch. Ges. Virusforsch. 29(4):343-360, 1970.

Compared with control primary cells, human amnion cells transformed by SV40 showed increased resistance to infection with poliovirus (PV). This resistance was manifested as a delay and decrease in virus production, decrease in cytopathic effect, inefficient formation of infectious centers and lack of PV plaque formation on monolayers of transformed cells. This resistance was ascribed to inefficiency in the initiation of infection. No difference was seen between transformed and control cells with respect to adsorption, penetration or eclipse of PV. Interferon could not be detected in transformed cells before or after infection with PV.

70-2455 ESTABLISHED LINES OF SV40-TRANSFORMED HUMAN AMNION CELLS. (E.) Gaffney, E. V. (Pennsylvania State U., University Park), J. Fogh, L. Ramos, J. D. Loveless, H. Fogh and A. M. Dowling. Cancer Res. 30(6):1668-1676, 1970.

11 lines were established from 5/200 cultures representing 22 strains of SV40-transformed human amnion cells in "crisis." A comparison of 5 lines showed that a larger number of chromosomes (80-100) was correlated with an increase in polycentric and new chromosome varieties, a decrease in acentric fragments and minute chromosomes, a shorter population doubling time and an epithelial-like morphology. The lines with the lowest chromosome numbers (50-60) were more fibroblastic. The 1 line which stopped producing virus 115 days after recovery contained the largest number of chromosomes and the highest percentage of telocentric chromosomes. Perikaryon formation between cells of this line and CV-1 cells resulted in the production of SV40. The cells were susceptible to infection with either SV40 or viral DNA. It is emphasized that 4/5 cell lines were cultured in the presence of mycoplasma infection or SV40 antiserum.

2456 SIMIAN PAPOVAVIRUS 40 TRANSFORMATION OF CELLS FROM CANCER PATIENT WITH XY/XY KLINEFELTER'S SYNDROME. (E.) Mukerjee, (U. Texas Med. Branch, Galveston), J. Bowen and D. E. Anderson. Cancer Res. 30(6):1769-1772, 1970.

Chromosome studies of WBC and fibroblast cultures from a 38-yr.-old man with Klinefelter's syndrome and lung cancer revealed that 52% of the WBC and 3 of the fibroblasts had a modal number of 46 chromosomes, a normal XY karyotype, while 45% of the WBC and fibroblasts had 47 chromosomes and an XXY sex chromosome complement. Frequency of transformation of fibroblasts by SV40 was $28.4/10^4$ cells for XXY strains and $9.7/10^4$ cells for XY strains. Cells from 4 control cultures had transformation frequencies of $1.7-3.3/10^4$ cells. Histological examination of lung tumor sections revealed that 3% of the tumor cells were positive for sex chromatin, indicating the tumor had an XXY sex chromosome constitution. These findings suggest that cells from this pt. are more susceptible to transformation than cells from normal individuals and indicate that the XXY strain is more susceptible to transformation than the XY strain from the same pt. It is not known whether the increased increase in susceptibility of the XY cell line resulted from terminal lung cancer or from some other cause.

57 DETECTION OF HUMORAL ANTIBODY RESPONSE TO POLYOMA TUMOR-SPECIFIC CELL-SURFACE ANTIGEN. (E.) Ting, C.-C. (NCI, Bethesda, Md.) and B. Herberman. J. Nat. Cancer Inst. 37:729-737, 1970.

Humoral antibody response to polyoma tumor-specific cell-surface antigen was detected in a 1:4 serum dilution with an isotopic anti-polyoma antigen method. Antisera were prepared by immunization of 3-4-mo.-old male C3H/HeN mice by s.c. or i.p. inj. with a subthreshold

dose (1×10^4 cells) of viable polyoma 4198 tumor cells (1 admin./week \times 2 mo.). Animals were bled from the retro-orbital sinuses 2-4 weeks after the last inj. Some of the mice received a booster inj. 2 mo. after the last inj. of tumor cells. With the isotopic anti-globulin method some of these antisera gave positive reactions with cultures of syngenic or allogenic polyoma tumor cells (polyoma 4198, polyoma 89, 3T3-Py), but not with nonpolyoma tumor cells or with normal mouse cells. These results cannot be attributed simply to increased immunoglobulin levels resulting from hyperimmunization. Since curves obtained from absorption of these antisera on polyoma 4198, polyoma 89 and 3T3-Py cells were arithmetically superimposable, it is concluded that the surface antigens in these 3 lines of polyoma tumor cells are identical and differ from those on nonpolyoma cells. Quantitative determinations demonstrated that polyoma 4198 cells had about 3-fold higher antigenic density than polyoma 89 and almost 6-fold that of 3T3-Py.

70-2458 A NEW TYPE OF VARIATION AMONG THE POLYOMA VIRUSES CHARACTERIZED BY CYTOPLASMIC ACCUMULATION OF CAPSID ANTIGEN. (E.) Hare, J. D. (U. Rochester Sch. Med. Dent., N. Y.). Virology 40(4):978-988, 1970.

Immunofluorescent examination of mouse embryo cells infected with 3049/PIB₂ strain of polyoma virus (PV) demonstrated capsid (C) antigen in the cytoplasm (Cyc⁺) 18 hours post-infection (p.i.) followed by its gradual appearance in the nucleus (20-24 hours p.i.). Comparison with 210 and 1p-S strains of PV showed the difference in C antigen distribution was strain-specific. Tumor antigen and infectious virion synthesis was normal and DNA synthesis inhibition inhibited C antigen formation. Study of several derivatives and isolates of the 3049 strain demonstrated the stability of Cyc⁺ particles. Studies of the effects of 5-fluorodeoxyuridine (FUDR; 15 μ g/ml) on the appearance of C and T antigens after infection with both 3049 and 1p-S viruses indicated C protein synthesis was controlled by a similar mechanism in both Cyc⁺ (3049) and Cyc⁻ (1p-S) strains; these were related to replication of the parental DNA molecule as suggested in the case of other animal viruses, such as adenovirus.

70-2459 LYSOSOMAL FACTORS RESPONSIBLE FOR THE RESISTANCE OF TRANSFORMED CELLS TO REINFECTION WITH HOMOLOGOUS VIRUS. (Rus.) Bykovskii, A. F. (N. F. Gamalei Inst. Epidem. Microbiol., Moscow) and I. S. Irin. Vop. Virus. 14(3):298-301, 1969.

Electron microscope study of tissue culture strains 866 (embryonic hamster cells transformed by polyoma virus) and 874 (hamster tumor cells induced with polyoma virus), 24 hours after

infection with polyoma virus (strain 2510 Eddy, viral titer of 10^8 TCID₅₀/0.2 ml), showed that enormous numbers of virus particles accumulated in many lysosomes. Polyoma virus was actively destroyed in the lysosomes, as seen by a decrease in the electron density of the nucleoids and destruction of the viral capsid. Hollow and tubular forms of polyoma virus were also present. Within 48-72 hours after infection the number of lysosomes containing disintegrating virions increased and complete destruction of polyoma virus apparently occurred in some of the lysosomes. No free virus particles were found in either the nuclei or the cytoplasm of these cells after infection. Unsuccessful attempts were made to demonstrate viral development within the nucleus by electron microscopy, the fluorescent antibody method, and virological methods. It is suggested that virus-specific changes in lysosome permeability are produced by virus-specific changes in the antigenic and physicochemical properties of lysosome membranes which are similar to virus-specific changes found in the cell membrane.

70-2460 NEOPLASTIC TRANSFORMATION OF HAMSTER ASTROCYTES AND CHOROID PLEXUS CELLS IN CULTURE BY POLYOMA VIRUS. (E.) Shein, H. M. (McLean Hosp. Res. Labs., Belmont, Mass.). J. Neuropath. Exp. Neurol. 29(1):70-88, 1970.

Cell cultures prepared from fetal hamster brains were transformed 120-150 days after inoc. with the small plaque Toronto strain of polyoma virus. Giant, multiple and budding nuclei and clumping of chromosomes at metaphase were noted in more than 90% of the cells in 3/6 early subcultures of polyoma-transformed brain cell lines. Polyoma virus-specific nuclear neoantigen (T antigen) was found in 1-5% of the nuclei in 4/5 transformed cell lines by indirect fluorescent antibody staining. Grade I and II astrocytomas were induced at the site of inoc. by s.c. inj. of newborn hamsters with 4 transformed cell lines containing T antigen. Pulmonary and renal metastases were observed 3-4 weeks after inoc. with 3/4 lines and liver and spleen metastases were observed with 1/4 cell lines; no cerebral metastases developed after inoc. with any of these cell lines. Astrocytomas induced by inoc. with 3 of these transformed cell lines were either pure or mixed with smaller areas whose structure was consistent with choroid plexus papilloma, adenocarcinoma, or undifferentiated carcinoma. The cell line which had produced spleen and liver metastases induced choroid plexus papillomas, adenocarcinomas and undifferentiated carcinomas mixed with much smaller areas of astrocytomas. When later tissue culture passages or cells from primary s.c. hamster tumors recultured in vitro were inj. s.c., more undifferentiated astrocytomas (grades III and IV) were produced. The entire histological range of astrocytomas was produced by s.c. or intracerebral inoc. of hamsters with cloned cells derived from 1 of the transformed cell lines.

70-2461 THE INTERACTION OF POLYOMA VIRUS WITH MOUSE-HAMSTER SOMATIC HYBRID CELLS. (E.) Basilico, C. (New York U. Sch. Med., N. Y.), Y. Matsuya and H. Green. Virology 41(2):295-305, 1970.

Somatic cell hybrids have been made between the hamster subline T6a, a hypoxanthine-guanine phosphoribosyl transferase-deficient derivative of BHK cells, and 3T3-4(E) or 3T3-4(C2F), thymidine-kinase-deficient sublines of the 3T3 mouse line. In clones isolated from these hybrids the ratio of mouse to hamster chromosomes ranged from 0.10:1 to 2.39:1 and, in contrast to other mouse-hamster hybrids, the number of chromosomes remained essentially unchanged. Except for 2 hybrids with an excess of hamster chromosomes and a deficiency of mouse chromosomes, almost all of these hybrid cells were capable of supporting the growth of polyoma virus of the small plaque type (Toronto strain), as manifested by their synthesis of T antigen. A strong correlation was found between synthesis of viral antigen in the nucleus and cell death. This supports the hypothesis that cell killing by polyoma virus is due to the synthesis of viral capsid proteins. Viral DNA synthesis, measured by incorporation of ³H-labeled thymidine into viral DNA at various times after infection, was noted in all hybrids but those with excess hamster chromosomes and a deficiency of mouse chromosomes. Surviving cells from the permissive hybrids were resistant to superinfection since they did not produce any virus and were not killed. These survivors may be cells in which the mouse gene necessary for polyoma virus replication has been lost.

70-2462 MODIFICATION OF ONCOGENICITY IN BHL (BABY HAMSTER LUNG CELL CONTINUOUSLY CULTURED IN VITRO) BY VIRAL PERSISTENT INFECTION OR ONE PASSAGE IN VIVO. (Jap.) Miyake, S. (Kanazawa U. Cancer Res. Inst., Japan). Ann. Rep. Cancer Res. Inst. Kanazawa Univ. 3(2): 141-162, 1970.

Oncogenicity of baby hamster lung (BHL) cells infected with the PR 8 strain of myxovirus was low in hamsters immunized with PR 8 virus, but not those immunized with polyoma virus. BH6-PR 8 cells, after in vitro infection, showed irregular signs of viral multiplication during serial passage (as shown by hemagglutinin in culture media, staining with fluorescein antibody and cytopathic effect). These changes were reversed by the addition of anti-PR 8 serum to the culture medium. The low oncogenic BHL cells which had been passaged only in vitro regained their oncogenicity after 1 passage in vivo in the hamster. In vitro culture of BHL tumor cells resulted in significant oncogenicity, attributed to the newly modified cell membrane.

2463 LIGHT SATELLITE-BAND DNA IN MOUSE CELLS INFECTED WITH POLYOMA VIRUS. (E.) With, B. J. (Imperial Cancer Res. Fund Labs., London). J. Molec. Biol. 47(1):101-106, 1970.

Light satellite-band DNA, DNA from mouse tissue which has a lower density (1.69 g/ml) in cesium chloride than main-band DNA (1.701 g/ml), replicates very early in baby mouse kidney cells infected with large-plaque polyoma virus. Light satellite-band DNA was labeled with ^3H -thymidine 16 hours after infection while main-band DNA is labeled only after 16 hours. Experiments designed to determine the site of labeling of the DNA made after initiation of DNA synthesis in polyoma-infected cells showed that a small amount of DNA is first synthesized in the nucleus but 11 hours after infection and that this is quickly followed by replication of all the nucleolar DNA. It is likely that at least some of the nucleolar DNA synthesis observed is that of light satellite-band DNA.

2464 MECHANISM OF THE DEVELOPMENT OF A STABLE CARRIER SYSTEM OF L CELLS WITH POLYOMA VIRUS. (E.) Lombardi, P. S. (U. Rochester Sch. Med. Dent., N. Y.). P. Balduzzi, D. Hare and H. R. Morgan. J. Nat. Cancer Inst. 41(1):171-178, 1970.

The stability of the viral carrier state resulting from infection of Earle's L929 cells with polyoma virus (PV) was studied. Preliminary investigation ruled out variation in cell response or abnormalities of adsorption or penetration of the virus. The absence of T antigen production and of stimulation of DNA synthesis in most infected L cells suggested that the virus was probably not uncoated nor was the genetic message transcribed or translated. The viral DNA was uncoated, productive infection observed. It is concluded that carrier structures of L cells were a product of a resistance in most cells in the L cell culture to productive infection as a result of their ability to control uncoating of viral particles.

2465 ELECTRON MICROSCOPIC STUDIES OF POLYOMA DNA RELEASED IN PROTEIN MONOLAYERS. Vasquez, C. (New York U. Sch. Med., N. Y.), C. Kleinschmidt and C. Basilio. J. Molec. Biol. 43(2):317-325, 1969.

Reversible conformational changes occurred in polyoma DNA molecules when they were adsorbed on a protein film over a denaturing phase of 3M or 6M urea and 1M or 2M sodium chloride. A large-plaque variant, grown on baby kidney cells, and a small-plaque variant, grown on 3T3 cells, were used. After disruption of the viral capsids about 60% of the viral DNA appeared as a tangled skein having a diameter greater than that of the intact virus. With increasing time, 80% of the structures observed

were twisted rings, 15% were open and semi-open (presumably nicked) rings and 5% were linear. Since the percentage of open ring forms was virtually constant, it is suggested that some of the molecules are already nicked inside the virion. The percentage of linear forms did not increase with time either. These molecules are probably mouse DNA released from pseudovirions. At higher conc. of urea and sodium perchlorate the molecules were shorter and had fewer twists than at lower conc. At higher conc. DNA molecules started to collapse after 15 min. Collapse is probably a result of strand separation due to local denaturation. Similar results were obtained when 0.3 M ammonium acetate (pH 5.5) was used as the hypophase.

70-2466 ERYTHROCYTE RECEPTORS OF THE POLYOMA VIRUS. (Fr.) Sassy, C. (Health Serv. Res. Lab. Marseille, France), G. Meyer and J. Nicolli. C. R. Soc. Biol. (Paris) 163(12):2653-2657, 1969.

After extraction with butanol and removal of soluble polyoma virus inhibitor in the supernatant, human RBC membranes (O Rh+) showed 2 principal groups of virus receptors, the mucopolysaccharides containing sialic acid-binding myxovirus, and lipoprotein receptors of picornavirus and arbovirus. It is concluded that the receptors of polyoma virus belong to the mucopolysaccharide group.

70-2467 DEOXYRIBONUCLEOTIDE POOLS AND DEOXYRIBONUCLEIC ACID SYNTHESIS IN MOUSE EMBRYO CELLS INFECTED WITH THREE CLASSES OF POLYOMA VIRUS PARTICLES. (E.) Skoog, L. (Karolinska Inst., Stockholm), B. A. Nordenskjöld and U. Lindberg. J. Virol. 6(1):28-32, 1970.

Purification by equilibrium centrifugation of polyoma virus particles from mouse embryo cells resulted in 3 classes of particles upon examination for infectivity, ability to induce pools of DNA precursors and ability to stimulate DNA synthesis. The most infectious group, the virions (buoyant density 1.33 g/ml), showed greatest stimulation of the DNA synthesis mechanism. The empty particles (buoyant density 1.29 g/ml) showed no DNA-stimulatory activity. Particles of intermediate density, the pseudovirions, were also less active than virions. Virion production of infection was 50-fold greater than for pseudovirions. It is suggested that a relation of DNA synthesis to infection with polyoma virus is due to infective particles, infective particles.

70-2468 INDUCTION OF VIRUS MULTIPLICATION IN 3T3 CELLS TRANSFORMED BY A THERMOSENSITIVE MUTANT OF POLYOMA VIRUS. I. ISOLATION AND CHARACTERIZATION OF TS-A-3T3 CELLS. (E.)

Vogt, M. (Salk Inst. Biol. Studies, San Diego, Calif.). *J. Molec. Biol.* 47(3):307-316, 1970.

Mouse embryo fibroblasts susceptible to polyoma virus infection (3T3 cells) were transformed by infection with a thermosensitive mutant of polyoma virus, Ts-a. This transformation, which affected relatively few cells, was attributed to the virus rather than to spontaneous transformation because no transformed cells (Ts-a-3T3) were observed in controls, Ts-a-3T3 cells were as susceptible as nontransformed 3T3 cells to killing by polyoma virus, and derivatives of Ts-a-3T3 cells that lost the ability to produce virus reverted to an almost normal phenotype. All Ts-a-3T3 lines isolated continued to produce small amounts of virus when grown at 38.5° C. The amount of virus increased with time and reached a max. when cultures became confluent. This capacity to produce virus was shown to be a hereditary trait of Ts-a-3T3 cells rather than a result of continued reinfection. Virus production increased markedly when Ts-2-3T3 cultures were shifted to 31° C. By plating for infective centers, determining virus yields from single cells and the proportion of cells synthesizing viral capsid proteins, it was established that increased virus production was due to increased production by only a fraction of the cells. The proportion of virus-producing cells continued to increase as long as the culture was actively growing. It is suggested that conditions favorable for cell growth are essential to initiate viral replication.

70-2469 INDUCTION OF VIRUS MULTIPLICATION IN 3T3 CELLS TRANSFORMED BY A THERMO-SENSITIVE MUTANT OF POLYOMA VIRUS. II. FORMATION OF OLIGOMERIC POLYOMA DNA MOLECULES. (E.) Cuzin, F. (Pasteur Inst., Paris), M. Vogt, M. Dieckmann and P. Berg. *J. Molec. Biol.* 47(3):317-333, 1970.

The physical state and replication of viral DNA was analyzed when cultures of 3T3 cells, transformed with a thermosensitive mutant of polyoma virus (Ts-a), were shifted from 38.5° C, where very little virus is produced, to 31° C, where virus production rises sharply after 36 hours, and back again to 38.5° C. Cultures continued to produce viral DNA for at least 24 hours after they were shifted back to 38.5° C. The kinetics of ³H-labeled thymidine incorporation into viral DNA can be explained if the Ts-a function is needed in a unique event which initiates viral DNA replication in the transformed cell. Sedimentation through cesium chloride gradients showed that viral DNA synthesized at 31° C consisted of monomer (M), and superhelical closed circular dimer (D) and trimer (T) DNA. The oligomers accounted for 40% of total viral DNA. All 3 of these DNA forms infected secondary mouse embryo cultures. Thus, both D- and T-DNA molecules contained at least 1 complete polyoma genome equivalent. DNA-DNA

hybridization experiments confirmed the dimeric and trimeric nature of D- and T-DNA. However, the results of this test did not rule out the possibility that the oligomers contained unlabeled host DNA. Oligomers are not obligatory precursors of monomers and are not present in mature virions. Only small amounts of oligomers were synthesized after acute infection with either wild-type or Ts-a polyoma virus.

70-2470 GROWTH CHARACTERISTICS OF VIRUS-TRANSFORMED CELLS. MAXIMUM POPULATION DENSITY, INHIBITION BY NORMAL CELLS, SERUM REQUIREMENT, GROWTH IN SOFT AGAR, AND XENOGENEIC TRANSPLANTABILITY. (E.) Eagle, H. (Albert Einstein Coll. Med., Bronx, N. Y.), G. E. Foley, H. Koprowski, H. Lazarus, E. M. Levine and R. A. Adams. *J. Exp. Med.* 13(4):863-879, 1970.

Cell cultures transformed by SV40 (4 human, 1 monkey and 1 mouse cell lines), adenovirus Type 7 and a hybrid between adenovirus Type 7 and SV40 (both in African green monkey kidney cells) and polyoma virus (in baby hamster kidney cells) were compared. Viral transformation caused a significant increase in the max. cell population, but the magnitude of the increase varied widely according to the virus and cell culture used. The transformed cells were usually smaller than the parent cells and required significantly lower conc. of serum for sustained cell growth; superinoculation onto monolayers gave no clear relationship between growth capacity and susceptibility to inhibition by other cell types. The plating efficiency also varied widely. Only the polyoma-transformed hamster kidney cells were tumorigenic after inoc. into the cheek pouch of Syrian hamsters, or i.p. inj. in newborn hamsters. No tumors were produced by any cells inj. intracerebrally in newborn Swiss mice.

70-2471 PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY IN CHRONIC LYMPHATIC LEUKEMIA - CAUSED BY POLYOMA VIRUS? (E.) Rausing, A. (Malmo Gen. Hosp. Path. Inst., Sweden) and U. Axelsson. *Scand. J. Haemat.* 7(3):184-194, 1970.

A 57-yr.-old man with chronic lymphatic leukemia (duration of 6 yr.) developed rapidly progressing bilateral loss of vision resulting in blindness, severe depression, apathy and left-sided hemiparesis, progressing to coma and death. Autopsy revealed extensive changes typical of progressive multifocal leukoencephalopathy (PML) in the brain and spinal cord. Negative staining revealed many clusters of particles with regular groups of 10-40 virions (38-43 nm size) arranged in a crystalline pattern. Morphology of these virions was compatible with papova virions of the polyoma-type.

70-2472 THE FINE STRUCTURE OF EQUINE PAPILLOMAS AND THE EQUINE PAPILLOMA VIRUS. (E.)

ulton, R. E. (U. Toronto Sch. Hyg., Ontario, Canada), F. W. Doane and L. W. Macpherson. J. Ultrastruct. Res. 30(3-4):328-343, 1970.

from combined light and electron microscopy studies of the sequence of viral development in quine papillomas, it has been demonstrated that quine papilloma virus, on the basis of its morphology and cellular location, is a papovavirus. quine papilloma virus, like other papilloma viruses, appears to replicate in the nucleus of epidermal cells. Examination of slices from quine papillomas showed that the stratum granulosum of the epidermis was the deepest layer in which the virus was found; virus was scattered throughout the nuclei and was occasionally found in association with the nucleolus. Virus particles, often forming isolated nuclear aggregates, were more numerous in the stratum granulosum. Closely packed arrays of virus were embedded in dense keratinous material in the stratum corneum. Electron microscopy of negatively stained viruses from papillomatous tracts revealed that the viral capsid consists of well-defined capsomeres which are arranged in accordance with icosahedral (5:3:2) symmetry. The mean diameter of intact particles was 57.2 mμ, a value within the range of 50-58 mμ reported for papilloma viruses of other species. The total number of morphological units present could not be determined.

2473 DETERMINATION OF MITOTIC ACTIVITY IN GROWING PAPILLOMA CELLS, INDUCED BY SHOPE VIRUS IN DOMESTIC RABBITS, UNDERGOING KERATINIZATION. (Fr.) Croissant, O. (Pasteur Inst., Paris) and G. Orth. C. R. Acad. Sci. [D] Paris 270(21):2609-2612, 1970.

Irregular and generally abnormal mitotic activity was found in the stratum granulosum of growing papillomas induced in rabbits by Shope papilloma virus. Labeled DNA was found in chromosomes of the stratum granulosum 2-3 hours after inj. of ³H-labeled thymidine into the base of the tumors. This confirms that keratinization, manifested as the appearance of keratohyalin granules, was not associated with complete inhibition of mitosis and suggests that rather highly differentiated chromosomal DNA was either partially or completely synthesized after keratohyalin granules appeared. The rate at which labeled DNA appears seems to be the same in the middle and lower thirds of the stratum granulosum.

2474 AN IN VITRO MEASURE OF CELLULAR IMMUNITY TO FIBROMA VIRUS. (E.) Tompkins, W. A. F. (Baylor Coll. Med., Houston, Tex.), C. Adams and W. E. Rawls. J. Immun. 104(2):502-510, 1970.

Inhibition of migration of peritoneal exudate macrophages was used to measure cell-mediated immunity to Shope fibroma virus (SFV) infection

in New Zealand White rabbits. Capillary tube migration of macrophages from rabbits immune to SFV was inhibited by antigens prepared from rabbit kidney cells infected with SFV. This inhibition was not seen with macrophages from non-immune rabbits or antigens prepared from non-infected rabbit kidney cells. The time after infection of donor rabbits, when sensitized exudate cells were obtained, correlated with the onset of a cutaneous delayed hypersensitivity reaction to SFV. It is concluded that this test measures specific antigens associated with the cell surface.

70-2475 CELLULAR DEOXYRIBONUCLEIC ACID SYNTHESIS AND LOSS OF CONTACT INHIBITION IN IRRADIATED AND CONTACT-INHIBITED CELL CULTURES INFECTED WITH FIBROMA VIRUS. (E.) Tompkins, W. A. F. (Baylor U. Coll. Med., Houston, Tex.), D. L. Walker and H. C. Hinze. J. Virol. 4(5):603-609, 1969.

After infection with the Patuxent strain of Shope rabbit fibroma virus, similar morphological changes occur in irradiated cultures of domestic rabbit kidney (DRK) cells, in which cell division was blocked by exposure to 5000 r of ionizing radiation, and in nonirradiated DRK cells, in which cell division was blocked by cell crowding and serum deprivation. These changes consisted of cell elongation and loss of contact inhibition, as manifested by disorientation and multilayering of the cells. Foci of piled-up cells were observed 6 days after infection. In contrast to nonirradiated cultures, in which the cells proliferated after an initial 45% reduction in the population, cell growth slowly declined in irradiated cultures. Viral DNA synthesis, determined autoradiographically by incorporation of ³H-labeled thymidine, reached a max. 12 hours after infection in both irradiated and nonirradiated cultures. After an initial inhibition of nuclear incorporation, a sharp increase occurred. This surge in nuclear incorporation was especially marked in cultures blocked by a combination of contact inhibition and serum deprivation. It is suggested that nuclear synthesis comes under some form of viral control or that nuclear synthesis is markedly influenced by viral effects on other parts of the cell. Morphological changes and loss of contact inhibition became apparent at about the same time that nuclear DNA synthesis increased in infected cells.

70-2476 EFFECT OF PERSISTENT FIBROMA VIRUS INFECTION ON SUSCEPTIBILITY OF CELLS TO OTHER VIRUSES. (E.) Padgett, B. L. (U. Wisconsin, Madison) and D. L. Walker. J. Virol. 5(2):199-204, 1970.

Shope fibroma virus (Patuxent strain) produced persistent cytoplasmic infection accompanied by morphological changes in primary rabbit kidney

(RK) cells and in serially cultivated rabbit kidney (DRK₃) cells. The response of these cells to superinfection with other viruses was compared to that of control cells by determining plaque production and the virus yield of superinfecting viruses. The growth of other pox viruses (myxoma and vaccinia) was greatly inhibited in cells infected with fibroma virus, whereas the growth of unrelated DNA viruses (pseudorabies and herpes simplex) was virtually unaffected. Some RNA viruses, poliovirus 1 and Coxsackie virus B1, did not produce plaques on either RK or fibroma-infected RK cells, while the growth of other RNA viruses (vesicular stomatitis virus, encephalomyocarditis virus, Sindbis virus and Newcastle disease virus) was enhanced in fibroma-infected RK cells. None of these latter RNA viruses produced any infectious progeny in DRK₃ cells, but they all formed plaques and produced good yields in DRK₃ cells persistently infected with fibroma virus. This phenomenon, called facilitation, results from the infection of DRK₃ cells by fibroma virus. Changes in the adsorption or eclipse of the superinfecting virus played no role in either interference or facilitation.

70-2477 GROWTH KINETICS OF YABA TUMOR POXVIRUS AFTER IN VITRO ADAPTATION TO *Cercopithecus* KIDNEY CELLS. (E.) Yohn, D. S. (Ohio State U., Columbus), F. R. Marmol and R. G. Olsen. J. Virol. 5(2):205-211, 1970.

Yaba tumor poxvirus, adapted to continuous in vitro cultivation in monolayers of green monkey kidney cells, replicates more efficiently at 35° C than at 37° C. At 35° C the minimum replicative cycle was 35 hours when cultures were inoc. with 135 FFU/cell, but max. virus yields were not obtained until 75 hours postinfection (p.i.). Viral DNA synthesis, detected by cytoplasmic incorporation of ³H-thymidine, occurred 3 hours p.i. and was preceded by synthesis of saline-soluble nonstructural antigens at 2 hours p.i. Synthesis of these antigens was apparently not inhibited by arabinofuranosyl cytosine (ara-C) which inhibits DNA synthesis. Synthesis of two structural virus antigens, detected 5 hours p.i., was not completely inhibited by ara-C even though the onset of DNA synthesis preceded structural antigen synthesis by 2 hours. This suggests that parental Yaba DNA may function in the translation of some of the structural antigens under conditions in which progeny DNA synthesis is inhibited. The temperature sensitivity of Yaba tumor poxvirus at 37° C is not due to a decrease in virus adsorption but appears to be due to the temperature-sensitivity of one or more enzymes involved in DNA synthesis. It is also possible that the population of this virus might be heterogeneous with regard to temperature-sensitivity, but no experimental evidence to support this hypothesis has been obtained.

70-2478 BURKITT'S LYMPHOMA: AN ELECTRON MICROSCOPE STUDY. (Rus.) Avtsyn, A. P. (Sci. Res. Inst. Human Morphol., Moscow), A. A. Zhavoronkov and V. A. Shakhlamov. Ark. Pat. 32(4):44-50, 1970.

Electron microscope examination of biopsy sections of a Burkitt's lymphoma showed 2 virus-like particles. The first type of particle was found in both the nuclei and the cytoplasm of the small lymphoblasts (diameter of 5-7 μ). Other particles, found in the nuclei on transverse and longitudinal sections, were 30 mμ in diameter, with an optically dense core (15 mμ in diameter) and a clear aureola. In addition, particles resembling mature herpes virus were found in the cytoplasm of tumor cells and capillary endothelial cells. The diameter of these particles ranged from 50-60 mμ. The small size of these particles may be due to tissue shrinkage and to the type of embedding medium used. Herpes virus was commonly found, particularly in cells of the hematopoietic system. It is suggested that one of these 2 viruses might be defective and require a helper virus for the synthesis of membranes or other structures necessary for complete viral replication.

70-2479 PRESENCE OF EB VIRUS NUCLEIC ACID HOMOLGY IN A "VIRUS-FREE" LINE OF BURKITT TUMOUR CELLS. (E.) zur Hausen, H. (U. Wurzburg Inst. Virol., Germany) and H. Schulte-Holthausen. Nature (London) 227(5255):245-248, 1970.

Study of DNA from purified Epstein-Barr (EB) virus, a herpes-type virus, and nucleic acid derived from the Raji line of Burkitt tumor cells demonstrated that this "virus-free" line actually contains about 6 EB virus genome equivalents/cell along with virus-specific messenger RNA. The Raji line, isolated from a Burkitt lymphoma, was tested for EB virus specific immunofluorescence and was subjected to virus concentrating procedures after prolonged labeling with ³H-thymidine. Both tests for EB virus were negative. Hybridization of DNA from the Raji line with 44S EB virus ³H-labeled DNA, with DNA from Nil-2, KB, and P3HR-1 cells used as controls, showed that Raji cells contained an av. of 6 EB virus DNA equivalents/cell. Preliminary studies revealed that Raji RNA and RNA from P3HR-1 cells were hybridized to a similar degree by DNA from EB virus. It appears that Raji cells synthesize an EB virus specific RNA, although additional research is needed to characterize this RNA and to determine the extent of its transcription.

70-2480 IMMUNOFERRITIN AND IMMUNOFLOUORESCENT STUDIES WITH EPSTEIN-BARR VIRUS AND HERPES SIMPLEX VIRUS BY USE OF HUMAN SERA AND HYPERIMMUNE RABBIT SERA. (E.) Hampar, B. (NCI,

ethesda, Md.), P. Gerber, K. C. Hsu, L. M. Santos, J. L. Walker, R. F. Sigüenza and G. A. Mills. J. Nat. Cancer Inst. 45(1):75-85, 1970.

erritin (Fer)- or fluorescein (Fl)-labeled anti-
era from rabbits immunized with Epstein-Barr
virus (EBV) from Burkitt lymphoma cells and a
similarly-labeled human EBV-positive serum were
tested against EBV-infected cells. The human serum
and Fer-labeled rabbit sera reacted with EBV
capsids; the Fl-labeled human serum, only, reacted
with EBV-infected cells. Rabbit anti-herpes
simplex virus (HSV) sera reacted with capsids and
EBV-infected cells in the same manner as anti-
EBV rabbit sera did. It is concluded from further
immunoferritin studies that EBV and HSV do not
have common or cross-reacting capsid surface
antigens.

0-2481 DIFFERENTIAL REACTIVITY OF HUMAN SERUMS
WITH EARLY ANTIGENS INDUCED BY EPSTEIN-
BARR VIRUS. (E.) Henle, W. (Child. Hosp.,
Philadelphia, Pa.), G. Henle, B. A. Zajac, G.
Carson, R. Waubke and M. Scriba. Science
199(3941):188-190, 1970.

onc. suspensions of Epstein-Barr virus (EBV;
prepared from culture media of the HRI-K subline
P3J Burkitt's lymphoma (BL) cells), when used
inoc. 64-10 (myelogenous leukemia) or Raji BL
cultures, caused abortive infections (early
antigens were synthesized, but not viral capsid
antigens). Sera from pts. with infectious
mononucleosis, BL, or nasopharyngeal carcinoma
were subjected to indirect immunofluorescence,
resulting in detection of antibodies to early
antigens. These antibodies were seldom present
in other sera regardless of elevated antibody
titers to EBV when assayed on EB3 BL cells.
Early antigen synthesis was prevented by these
antibodies in cases where the serum and virus
were mixed prior to inoc. It is concluded that
antibodies to early antigens may reflect current
or recent virus-associated disease processes.

-2482 INFECTIOUS MONONUCLEOSIS IN ACUTE
LEUKEMIA WITH RISING EPSTEIN-BARR
VIRUS ANTIBODY TITERS. (E.) Deardorff, W. L.,
P. Gerber and W. R. Vogler (Emory U., Atlanta,
Ga.). Ann. Intern. Med. 72(2):235-240, 1970.

21-yr.-old male college student who presented
with fever, a negative heterophil test and
x-ray findings of acute myeloblastic leukemia
developed periorbital edema, atypical peripheral
blood lymphocytes, and high infectious mono-
nucleosis (IM) heterophil titer after 8 weeks.
Examination of serum taken at presentation
showed no Epstein-Barr (EB) virus antibodies,
but when the heterophil titer was max. EB virus
antibodies appeared in the serum and subsequently
rose and remained at high levels. This is the
fourth case of IM occurring spontaneously during
the course of acute leukemia. The data fail to

demonstrate how one disease might have altered
the course of the other.

70-2483 IMMUNOFLUORESCENCE IN THE STUDY OF
MAREK'S DISEASE. I. DETECTION OF
ANTIGEN IN CELL CULTURE AND AN ANTIGENIC COMPARI-
SON OF EIGHT ISOLATES. (E.) Purchase, H. G.
(Reg. Poultry Res. Lab., East Lansing, Mich.).
J. Virol. 3(6):557-565, 1969.

In chick kidney cells infected with a stock
cellular preparation of the JM strain of Marek's
disease (MD), infected cells were detected after 24
hours by immunofluorescence but no morphological
foci were seen. By 7 days post-infection the same
number of infected areas were detected by both
methods and the fluorescent foci coincided with the
morphological foci; thus, the antigens detected
in cell culture by indirect fluorescent antibody
(FA) testing are induced by the virus which
caused the characteristic cytopathology. Cell
cultures inoc. with 8 different isolates of MD
and tested in all combinations with sera prepared
against the same isolates showed antigens were
indistinguishable from one another, possibly
because the strains were antigenically identical
or due to a common antigen or contaminant in
each. The FA test can detect MD antigen before
cytopathological areas develop in cell culture;
however the small size of the area usually
examined precludes its use in initial isolations
in which only a small number of infectious units
are present in the inoculum.

70-2484 VIRUS-SPECIFIC IMMUNOFLUORESCENT AND
PRECIPITIN ANTIGENS AND CELL-FREE
VIRUS IN THE TISSUES OF BIRDS INFECTED WITH
MAREK'S DISEASE. (E.) Purchase, H. G. (US Dept.
Agric. Reg. Poultry Res. Lab., East Lansing,
Mich.). Cancer Res. 30(6):1898-1908, 1970.

An investigation of immunofluorescent (IF) and
precipitin antigens and infectious virus in a
variety of organs from inbred and cross-bred
chickens inoc. with Marek's disease virus (MDV)
demonstrated a close association between the
presence of antigens and cell degeneration and
necrosis. At age 1 day or 3 weeks, chicks were
inoc. intraabdominally with blood from chickens
infected with the JM or RPL39 strains of MDV.
Using serum from chickens hyperimmunized with
MDV, IF antigens were detected by the direct
fluorescent antibody method in superficial cells
of the epithelium of the feather follicles,
lungs, follicles of the bursa of Fabricius,
thymus, spleen and cecal tonsil, but were not
found in any of the tumors. Differences in the
distribution of IF antigen from that reported
in the literature may be due to differences in
the strains of chicken, in the virus or in the
specificity of the conjugates. Precipitin antigen,
which may have been identical to IF antigen,
was detected by the agar gel microprecipitin
test. Precipitin antigen was found in all the

above organs with the exception of the cecal tonsil. Filterable virus, infectious for chick kidney cell cultures, was recovered from skin extracts but not from extracts of the lungs, bursa or thymus.

- 70-2485 COMBINED FLUORESCENT-ANTIBODY AND ELECTRON MICROSCOPY STUDY OF MAREK'S DISEASE VIRUS-INFECTED CELL CULTURE. (E.) Nazerian, K. (Reg. Poultry Res. Lab., East Lansing, Mich.) and H. G. Purchase. J. Virol. 5(1):79-90, 1970.

Combined fluorescent antibody and electron microscopy studies of duck and chick embryo fibroblast (EF) cultures infected with the JM strain of Marek's disease virus (MDV) showed herpes virus particles in the cells with immunofluorescent (IF) antigen. Cytoplasmic studies showed 2 morphologically distinct IF antigens, a granular one in the perinuclear region which did not contain virions and a diffuse antigen found throughout the cytoplasm with naked virions occasionally present. IF antigen was more often found in the cytoplasm than in the nucleus. It is concluded that the IF antigens of MDV-infected EF cultures are virus-specific.

- 70-2486 CELL-FREE TRANSMISSION AND IN VIVO REPLICATION OF MAREK'S DISEASE VIRUS. (E.) Nazerian, K. (Reg. Poultry Res. Lab., East Lansing, Mich.) and R. L. Witter. J. Virol. 5(3):388-397, 1970.

Clinical symptoms of Marek's disease (MD) were produced in cross-bred, 1-day-old chicks by i.p. inoc. with cell-free preparations of feather follicles from infected chickens. Herpes virions were found in the feather follicles and specific microplaques developed in cultures established from the kidneys of chicks inoc. i.p. with low-passage MD virus (JM strain) propagated in duck embryo fibroblast cultures. High-passage cultures of MD and an antigenically related herpes virus of turkeys were avirulent, probably because of the inability of these strains to replicate in the feather follicle. Low-passage strains of MD virus replicated in the epithelial cells of the germinative layer of the feather follicle epidermis, producing both intranuclear and round or diffuse cytoplasmic inclusion bodies in the infected cells. Virus was found at this site 2 weeks after inoc. and before the development of tumors or other gross lesions. A few enveloped and many nonenveloped herpes virions were found in the nucleus, while the cytoplasm contained mostly enveloped herpes virions usually found within the cytoplasmic inclusion bodies. About 80% of the extracellular virions were enveloped.

- 70-2487 ATTENUATION OF MAREK'S DISEASE VIRUS AND STUDY OF ITS PROPERTIES IN TWO DIFFERENT CELL CULTURES. (E.) Nazerian, K.

(Reg. Poultry Res. Lab., East Lansing, Mich.). J. Nat. Cancer Inst. 44(6):1257-1267, 1970.

When passaged in duck embryo fibroblasts (DEF), changes occurred in the morphology of microplaques produced by Marek's disease virus (MDV); by passage 100, pathogenicity of the virus for chickens was lost. However, MDV was reisolated from the kidneys of some chickens inoc. with cells from these later passages although no clinical signs or gross lesions were observed. Attempts to isolate MDV indirectly in chick embryo fibroblasts (CEF) were unsuccessful, but microplaque formation was extensive when CEF cultures were cocultivated with MDV-infected DEF cultures. Cell-free MDV was recovered from the growth medium of infected CEF; microplaques in this culture consisted of round and slightly elongated cells. No cell-free MDV was recovered in the growth medium of infected DEF, and microplaques consisted of syncytial cells. These morphological differences were specific to the type of cell and not to the strain of the virus. Microplaque development was inhibited in CEF, and particularly in DEF, cultures when 5-bromo-2'-deoxyuridine (5-BUDR) was added. The inhibitory effect of 5-BUDR was blocked by addition of thymidine to the medium. This blocking effect could either be due to substrate competition or to actual enhancement of MDV-DNA synthesis by thymidine.

- 70-2488 AUTORADIOGRAPHIC AND CYTOCHEMICAL STUDIES ON NUCLEAR AND CYTOPLASMIC INCLUSIONS OF DUCK EMBRYO FIBROBLASTS INFECTED WITH HERPES TYPE VIRUS ISOLATED FROM CHICKENS WITH MAREK'S DISEASE. (E.) Ono, K. (Osaka U. Res. Inst. Microb. Dis., Japan), S. Kato, N. Iwa and T. Doi. Biken J. 13(1):53-57, 1970.

Cultures of duck embryo fibroblasts (DEF) were inoc. with Biken A, B and C strains of a herpes-type virus (HTV) and foci developed within 3-5 days. The foci contained many round cells and multinucleated giant cells, with eosinophilic cytoplasmic (C) inclusions and herpes-type nuclear (N) inclusions. The C inclusions appeared to occur subsequent to formation of N inclusions; they were detectable in DEF cultures for 36 passages. Histological study of HTV-infected DEF showed that DNA synthesis occurred only in the nuclei; thus, C inclusions are not related to DNA synthesis. It is suggested that the significance of C inclusions in viral replication be further investigated.

- 70-2489 A PRELIMINARY REPORT ON THE SEROLOGY OF LUCKÉ AND BURKITT HERPES-TYPE VIRUSES: A SHARED ANTIGEN. Kirkwood, J. M., G. Geering, L. J. Old, M. Mizell and J. Wallace. Pp. 365-367 in Biology of Amphibian Tumors, Mizell, M. (Ed.). Springer-Verlag, New York, 1969, 484 pp. (Recent Results Cancer Res., Special Suppl.).

Investigation of the sera of a variety of amphibians revealed a natural antibody to herpes-type virus (HTV) in 9/115 normal Rana pipiens and 4/5 animals with tumors induced by the Lucké virus (L-HTV). Positive frog sera and rabbit anti-HTV sera gave reactions of identity in immunoprecipitation tests with L-HTV. Since purified Burkitt HTV (P3V) was strongly precipitated by rabbit anti-L-HTV serum, and since absorption of the rabbit anti-L-HTV serum with P3V eliminated precipitation against L-HTV, and Burkitt HTV, it is concluded that the Burkitt and L-HTV viruses are common antigens. Both rabbit and frog sera precipitated L-HTV, giving reactions of identity. Rabbit anti-L-HTV serum also precipitated the Burkitt P3V, giving reactions of identity with L-HTV. Rabbit anti-FV3 serum failed to react with L-HTV or Burkitt HTV.

2490 HERPESTYPE VIRUS LATENCY IN THE LUCKE TUMOR. Mizell, M., C. W. Stackpole and J. J. Isaacs. Pp. 337-347 in Biology of Amphibian Tumors, Mizell, M. (Ed.). Springer-Verlag, New York, 1969, 484 pp. (Recent Results Cancer Res., Special Suppl.).

The emergence of herpes-type virus (HTV) in the Lucké was studied in frog (Rana pipiens) anterior eyechambers receiving nodule transplants from a virus-free primary tumor. Low temperature environment of about 7.5° C was maintained. The presence of HTV was first observed after 9.5-10 weeks in 2 series (134) of frogs observed; the number of virus-containing cells increased to a plateau with about 20% infection after 14-16 weeks. To eliminate the possibility of extraneous viral origin, 58 R. clamitans and Bufo americanus eyechambers received transplants as above (same temperature), resulting in virus appearance after 9-9.5 weeks with subsequent virus production levels same as above. This induction of virus in tumor cells previously virus-free suggests a relatively complete viral genome in either a latent or masked state. Low temperature induction of virus in 'summer' tumor transplants maintained in foreign hosts suggests de novo production of virus within the transplanted tumor cells and eliminates the possibility of virus originating in other host tissue and subsequently migrates into the tumor cells for replication.

2491 REACTIVITY OF SERUM FROM FROGS AND OTHER SPECIES WITH A HERPESVIRUS ANTIGEN EXTRACTED FROM A BURKITT LYMPHOMA CULTURED CELL LINE. Fink, M. A., G. S. King and M. Mizell. Pp. 358-364 in Biology of Amphibian Tumors, Mizell, M. (Ed.). Springer-Verlag, New York, 1969, 484 pp. (Recent Results Cancer Res., Special Suppl.).

Positive results were obtained from immunodiffusion testing of sera from 1-3-yr.-old frogs against Epstein-Barr virus (EBV). The few frog

sera tested with frog antigen demonstrated a reaction of complete identity between antigen 'a' of EBV and the antigen of the herpes virus of the Lucké tumor. Neither the EBV nor the frog antigen reacted with the herpes simplex antibody, nor did positive frog sera react with herpes simplex antigen. When testing sera from domestic animals and primates with EBV, at least 1 animal of each species of the domestic animals tested (goat, cat, sheep, dog, horses, cow) reacted strongly with EBV antigen. The goat and horse sera tested reacted strongly with the frog antigen, the 2 sera reacted in a line of identity. A cat serum reacted weakly with frog antigen.

70-2492 HERPES-TYPE VIRUS OF THE FROG RENAL ADENOCARCINOMA. I. VIRUS DEVELOPMENT IN TUMOR TRANSPLANTS MAINTAINED AT LOW TEMPERATURE. (E.) Stackpole, C. W. (Sloan-Kettering Inst. Cancer Res., New York, N. Y.). J. Virol. 4(1):75-93, 1969.

Development of the herpes-type virus in renal adenocarcinomas from Rana pipiens was followed by electron microscopy and high-resolution autoradiography in eyechamber transplants of tumor maintained at 7.5° C for up to 27 weeks. Virus particles were first detected at 10 weeks in nuclei containing aggregates of dense granular material. Incorporation of ³H-thymidine into these aggregates and the absence of labeling in noninfected cells indicate that the aggregates contain newly synthesized viral DNA. Capsids enclosing double-shelled cores were labeled with ³H-thymidine before capsids with dense cores, and intermediate core forms were observed, suggesting that the double-shelled core is a precursor of the dense core. Particles with dense cores were observed while being enveloped by budding through the inner membrane of the nuclear envelope, and subsequently while being unenveloped in passing through the outer membrane into the cytoplasm. Virus particles in the cytoplasm acquired fibrillar coats and budded into vesicles from which they were released, in enveloped form, at the cell surface. Tubular forms and particles considerably smaller than virus particles were commonly found in infected nuclei. The tubular structures, observed in advanced infection, are considered to be aberrant virus-related forms. The smaller particles are surpluses of viral components which remain unincorporated into complete virus particles. This suggests that virus assembly may occur by chance association of components rather than by an intricate assembly mechanism.

70-2493 SIMULATED TRANSMISSION OF RENAL TUMORS IN OOCYTES AND EMBRYOS OF Rana pipiens. Tweedell, K. S. Pp. 229-239 in Biology of Amphibian Tumors, Mizell, M. (Ed.). Springer-Verlag, New York, 1969, 484 pp. (Recent Results Cancer Res., Special Suppl.).

Experiments were designed to simulate renal tumor transmission through both horizontal (from external source of infection) and vertical (through the embryo) routes. Subcellular cytoplasmic fractions of spontaneous renal tumors containing herpes-like virus were used to determine if the frog embryonic and larval periods are the natural infective period. Inj. of renal tumor cell fractions beneath the membranes of fertilized eggs or into tailbud embryos of Vermont *R. pipiens* produced tumors in 0/105 and 6/20 6-mo.-old and 3-mo.-old adults, resp. Tumor cell fractions placed in the culture water of recently hatched Wisconsin *R. pipiens* embryos for a period of 32-36 days produced no apparent effect on larvae. Nine of the experimental animals developed tumors before, during or after metamorphosis; many had no tumors after 1.5 yr. Spermatozoa inoc. with tumor virus fractions and used to fertilize normal eggs caused heavy mortality (only 15/570 receiving mitochondrial tumor fractions were living after 1 week), but failed to induce tumors in survivors. Latent renal tumors developed in young adults 5-12 mo. after oocyte exposure to tumor virus fractions in vivo during ovulation.

70-2494 LUCKÉ RENAL ADENOCARCINOMA: EPIDEMIOLOGICAL ASPECTS. McKinnell, R. G. Pp. 254-260 in Biology of Amphibian Tumors, Mizell, M. (Ed.). Springer-Verlag, New York, 1969, 484 pp. (Recent Results Cancer Res., Special Suppl.).

Examination of over 3367 leopard frogs collected from known Minnesota localities from 1965-1968, inclusive, revealed a seasonal variation in tumor prevalence: spring and fall frogs had a higher prevalence than summer frogs (5%, 4.4% and 0.14%, resp.). There was also a seasonal fluctuation of virus particles in tumors: prehibernating frogs had virus-free tumors, while all frogs emerging from hibernation demonstrated virus particles in their tumors. Renal tumors were detected in frogs from 9/15 Minnesota counties examined. Autopsy of 618 frogs from Stutsman county, North Dakota, 110 from Whiteman Dam, N. D. and 247 frogs from northern Louisiana showed no adenocarcinomas.

7 -2495 FINE STRUCTURE STUDIES OF CYTOPLASMIC VIRUSES ASSOCIATED WITH FROG TUMORS. Lunger, P. D. Pp. 296-309 in Biology of Amphibian Tumors, Mizell, M. (Ed.). Springer-Verlag, New York, 1969, 484 pp. (Recent Results Cancer Res., Special Suppl.).

Fine structural aspects of virus location (host cell type), general morphology, associated organelles and maturation events were studied in frog renal adenocarcinoma cells. Results show apparently icosahedral cytoplasmic viruses (135 mμ diameter) in stromal but not epithelial cells of 4/38 (10.5%) virus-containing renal adenocarcinomas. The formation of a spiney-

surfaced shell within a flocculent viroplasm was the first visible stage of maturation; as this shell became spheroid, the internal material assumed high electron density. Eventually the mature particles acquired an envelope derived from the cell plasma membrane.

70-2496 PLASMACYTOMA IN A *Rana pipiens*. Schochet, S. S., Jr. and P. W. Lampert. Pp. 204-214 in Biology of Amphibian Tumors, Mizell, M. (Ed.). Springer-Verlag, New York, 1969, 484 pp. (Recent Results Cancer Res., Special Suppl.).

An adult female *Rana pipiens*, implanted with a fragment of a typical Lucké renal cell carcinoma into the anterior chamber of the eye, developed a plasmacytoma in the thigh 2.5 mo. later. This is the first example of a plasmacytoma in a frog. The majority of neoplastic cells were plasma cells displaying varying degrees of protein storage. Many tumor cells contained double-walled tubular virus-like particles in their cytoplasm.

70-2497 COMPARATIVE STUDIES OF AMPHIBIAN CYTOPLASMIC VIRUS STRAINS ISOLATED FROM THE LEOPARD FROG, BULLFROG, AND NEWT. Clark, H. F., C. Gray, F. Fabian, R. Zeigel and D. T. Karzon. Pp. 310-326 in Biology of Amphibian Tumors, Mizell, M. (Ed.). Springer-Verlag, New York, 1969, 484 pp. (Recent Results Cancer Res., Special Suppl.).

Virus isolated from newts was compared with previously studied *Rana pipiens* isolates LT1-LT4 (recovered from efts), L4 and L5, and FV1-FV3, and with the similar isolate tadpole edema virus (TEV), recently isolated from bullfrogs (*Rana catesbeiana*). A study of 4 different lots of uninoc. adult newts revealed 15 isolates (T6-T20); 1 additional isolate (T21) was found. T isolates cross-reacted in neutralization tests with LT1, FV1 and TEV and resembled the FV, LT and L isolates in fine structure and in induction of cytopathic effect (formation of cytoplasmic inclusion bodies at 23° C incubation temperature). Each virus exhibited max. plaquing efficiency at 19-21° C with complete inhibition occurring at 33.6° C. Efts and toads became infected with viruses of both newt and frog origin. LT1, LT2, FV1 and TEV, but not L5 and L6, caused tumor development in toads. No isolates induced tumor in efts.

70-2498 INHIBITION OF CELLULAR DNA AND RNA SYNTHESIS IN KB CELLS INFECTED WITH FROG VIRUS 3 (FV3). (Fr.) Guir, J. (INSERM Inst. Bacteriol., Strasbourg, France), J. Braunwald and A. Kirn. C. R. Acad. Sci. [D] (Paris) 270(21):2605-2608, 1970.

At 37° C, cellular RNA and DNA synthesis were rapidly and completely inhibited in monolayers

of KB cells by infection with purified frog virus 3 (FV3). This inhibition was not associated with viral development, since 26-29° C is the optimum temperature for FV3. Extracts from non-infected BHK₂₁ cells, on which FV3 was grown, had no effect on cellular nucleic acid synthesis. When KB cells infected with FV3 were incubated for 6 hours at 37° and were then transferred to 26° C, the amount of viral DNA produced was almost as high as when infected cells were incubated at 26° C from the beginning.

70-2499 APPEARANCE, CHARACTERISTICS AND MALIGNANCY OF SOMATIC HYBRID CELLS BETWEEN L AND EHRLICH ASCITES TUMOR CELLS FORMED BY ARTIFICIAL FUSION WITH UV-HVJ. (E.) Murayama, F. (Osaka U. Res. Inst. Microb. Dis., Japan) and Y. Okada. Biken. J. 13(1):11-23, 1970.

A hybrid cell line was formed in HAT medium by fusion of Ehrlich ascites carcinoma (EAC) cells and an 8-azaguanine-resistant mutant of L cells (LAG) with UV-HVJ virus (not further identified). The hybrid (LE cells), which was detected 40 hours after fusion by labeling with ³H-hypoxanthine, exhibited a morphology intermediate between those of the parent cells. In contrast to the EAC cells, which did not grow in vitro under these conditions, the LE cells grew rapidly, with a generation time of 11.5 hours (compared to the 18 hours required by LAG). The chromosome numbers in LE-induced tumors in dd0 and C3H mice were 83 and 81, resp., about 10 less than the total number of chromosomes in the parent cell lines in both cases. LE cells contained surface antigens from both parent cells; when inj. i.p., LE cells produced sarcomas in dd0 and C3H mice after a 1-mo. latent period. The malignancy of the LE cells was shown to depend upon the malignancy of the EAC cells and was lower than that observed in the EAC cells. The reduced malignancy of the hybrid is probably not due to immunological inhibition induced by antigens on the hybrid cells. The capacity of LE cells to form large colonies in soft agar increased with time, but was not related to their oncogenicity.

70-2500 TUMORIGENIC ACTION OF BACTERIOPHAGE NUCLEIC ACID IN CULTURES OF SUNFLOWER TUMOR TISSUE (*Helianthus annuus*). (Fr.) Leff, J. Manhattan Coll., Bronx, N. Y.) and R. E. Wardsley. C. R. Acad. Sci. [D] (Paris) 270(20): 205-2507, 1970.

A preparations from *Agrobacterium tumefaciens* gave PS 8 induced tumors in sunflower and tobacco plants.

70-2501 BEHAVIOR OF VIRUS IN MALIGNANT DEGENERATION OF SKIN LESION IN EPIDERMODYSPLASIA VERRUCIFORMIS. (E.) Ruiter, M. (Utrecht, Netherlands) and P. J. van Mullem. Invest. Derm. 54(4):324-331, 1970.

Electron microscope examinations were made of 4 biopsies from the forehead of a 25-yr.-old male imbecile with epidermodysplasia verruciformis, who eventually developed an invasive intraepidermal squamous cell carcinoma. Histological features were similar to those of Bowen's disease or actinic keratosis. An intranuclear virus identical with or closely related to that of verruca vulgaris (the human wart virus) was observed in all 4 biopsies. No complete virus particles were found in the fully developed squamous cell carcinoma. The relatively small number of virus-infected cells in the intraepidermal carcinomas, the decreased tendency of the virus to differentiate in the form of crystalloid arrays, and the unusual spatial distribution of the virus particles, suggested that formation of complete virus was disturbed directly or indirectly by intraepidermal changes.

70-2502 EXPERIMENTAL INDUCTION OF LEUKOSIS IN MICE FOLLOWING DRINKING OF HUMAN BLOOD OF NEOPLASTIC DISEASES. (Jap.) Sawayama, K. (Shikoku Railroad Hosp., Japan). J. Karyopath. 12(3):145-162, 1969.

Inbred D103 and C57BL mice underwent drinking tests with blood from leukemia pts. and from pts. who had died of liver cancer; 3/10 mice developed leukosis (2 with successful serial transmission) after admin. of blood from pts. with chronic myeloid leukemia (1/2 pts.), carcinoma of the liver (1/1) or monocytic leukemia (1/1). No leukosis developed after admin. of blood from 7 pts. with acute lymphocytic (2) or myeloid (3) leukemia, chronic lymphocytic leukemia (1) or 1/2 with chronic myeloid leukemia. No leukosis was seen in controls given blood from 1 pt. with operated intestinal cancer, 1 with malignant hemangioma, 7 pts. with non-malignant diseases and 1 healthy subject. In dd mice, the 2 transmissible diseases were sub-acute myeloid leukosis. A filterable agent was demonstrated and easily replicated in HeLa and L cells. As replication of this unidentified virus is relatively easy, it is not considered to be a "passenger" virus.

70-2503 VIRAL NATURE OF HUMAN LEUKEMIA. (Rus.) Lapin, B. A. (Inst. Exp. Path. Ther., Sukhumi, USSR) and L. A. Iakovleva. Vestn. Akad. Nauk SSSR 25(5):60-71, 1970.

Fresh, whole heparinized or citrated blood from pts. with stem cell leukemia or with chronic myeloid leukemia in acute transformation was inj. (route not specified) into 23 hamadryas baboons, 13 rhesus macaques and into brown macaques. The macaques were 1-3 yr. old; 13/29 baboons were newborn. Some of the baboons and brown macaques developed a progressive leukemia-like disease which, in some of the baboons, had symptoms characteristic of human leukemia. Both

whole and filtered blood from brown macaques was passaged readily, but the disease produced in this way was reversible. Electron microscopic examination of blood cells from infected baboons and brown macaques showed the presence of viral particles (diameters ranging from 850-1200 Å) which replicated on the cell surface by budding. These virus particles were similar to those found in other animal leukemias. Similar virus particles were found in the blood cells of a male brown macaque inoc. with supernatant from ultracentrifuged urine from a leukemic baboon. Leukemia developed in some control baboons maintained in close contact with inoc. animals. These animals might have become infected by contact with urine. By means of indirect immunofluorescence, a cell-surface antigen was found in the blood of all animals with symptoms of leukemia, in some of the inoc. animals which remained asymptomatic and in some controls kept in contact with inoc. animals. This antigen appears to be specific as it was not found in controls inoc. with WBC from normal human or monkey donors, or with heated blood from leukemia pts. It is concluded that the virus causing leukemia in these animals is of human origin, since monkeys never develop spontaneous leukemia.

70-2504 TRANSMISSION OF FELINE FIBROSARCOMA VIRUS TO MARMOSET MONKEYS. (E.) Wolfe, L. (Rush-Presbyterian-St. Luke's Med. Ctr., Chicago, Ill.), R. McDonald, F. Deinhardt, S. Snyder and G. Theilen. Fed. Proc. 29(2):371, 1970.

79-2505 SOLUBILIZATION OF GROSS VIRUS-INDUCED CELL SURFACE ANTIGEN. (E.) Herberman, R. B. (NIH, Bethesda, Md.). Fed. Proc. 29(2):371, 1970.

70-2506 CLEAVAGE OF SIMIAN VIRUS 40 DNA BY BACTERIAL RESTRICTING ENZYMES. (E.)

Adler, S. P. (Johns Hopkins U. Sch. Med., Baltimore, Md.) and D. Nathans. Fed. Proc. 29(2):725, 1970.

70-2507 VARIATIONS IN ANTIGENICITY OF THE SAME CELL LINE (SV40 TRANSFORMED HAMSTER FIBROBLASTS) IN TISSUE CULTURE AND IN ANIMAL TUMORS. (E.) de Vaux Saint Cyr, C. (Sci. Res. Inst. Cancer, Villejuif, France). Fed. Proc. 29(2):372, 1970.

70-2508 CORRELATION BETWEEN SV40 RESCUE AND PRESENCE OF A PARAMYXO-LIKE VIRUS IN SV40-TRANSFORMED HAMSTER CELLS. (E.) Jensen, F. C. (Wistar Inst., Philadelphia, Pa.), F. S. Lief and K. Hummeler. Fed. Proc. 29(2):372, 1970.

70-2509 THE DEVELOPMENT OF SV40 ANTIGENS IN HUMAN AMNION CELLS. (E.) Gaffney, E. V. (Sloan-Kettering Inst., New York, N. Y.) and J. Fogh. Fed. Proc. 29(2):372, 1970.

70-2510 MYCOPLASMA INFLUENCE ON HUMAN AMNION CELLS TRANSFORMED BY SV40. (E.) Fogh, J. (Sloan-Kettering Inst., New York, N. Y.). Fed. Proc. 29(2):559, 1970.

70-2511 INDUCTION OF CELO VIRUS OF SARCOMAS AND HEPATOMAS IN HAMSTERS, AND OF "T" ANTIGEN IN LYTICALLY INFECTED CHICK KIDNEY CELLS. (E.) Anderson, J. (Baylor Coll. Med., Houston, Tex.), K. J. McCormick and J. J. Trentin. Fed. Proc. 29(2):559, 1970.

70-2512 MOBILIZATION OF DNA SYNTHESIZING ACTIVITY OF STATIONARY HAMSTER CELLS BY TYPE 12 ADENOVIRUS (Ad12). (E.) Zimmerman, J. (Rutgers Med. Sch., New Brunswick, N. J.), W. A. Strohl and K. Raska, Jr. Fed. Proc. 29(2):309, 1970.

See also abstract nos: 2126,2135,2136,2138,2139,2140,2141,2142,2143,2144,2145,2146,2147,2148,2149,2150,2184,2561,2576,2588,2589,2591,2631,2633,2634,2643,2647,2648,2650

0-2513 MALIGNANT NEOPLASMS IN CERTAIN COUNTRIES. (E.) World Health Organization. d. Hlth. Stats. Rep. 22(2):69-166, 1969.

A compilation is given of the number of registered cases and morbidity rates/100,000 population by sex, age and site of 53 malignant neoplasms in 10 countries, continuing sets of data compiled at different times from 1958 to 1968.

0-2514 CANCER IN BRAZZAVILLE, THE CONGO. (E.) Tuyns, A. J. (Int. Agency Res. Cancer, Paris, France) and P. Ravisse. J. Nat. Cancer Inst. 44(5):1121-1127, 1970.

During 1965 and 1966, 508 malignant tumors were reported by hospitals in the Republic of Congo (mostly in Brazzaville and Pointe Noire). The group of pts. included 243 males and 262 females (10 males and 9 females were in the 0-14-yr. age group). The most prevalent tumor in males and the fourth most prevalent tumor in females was liver cancer (40.7% and 7.6% of all tumors, resp.). The minimum annual crude incidence rates for liver cancer were 11/100,000 males and 4/100,000 in females; these represent the highest known crude incidence rates after Zaire (Lourengo Marques) and the Bantu population of Johannesburg.

0-2515 CANCER MORTALITY TRENDS AND CANCER CONTROL METHODS IN THE RUMANIAN SOCIALIST REPUBLIC (R.). (Rum.) Georgescu, D. C. (Inst. Oncol., Bucharest). Oncol. Radiol. 15(2):225-253, 1969.

In 1931, the mortality rate due to neoplasms of the total population of Rumania was 38/100,000/yr. (93.8 and 25.7 for the urban and rural areas, resp.); corresponding figures for 1967 were 120.8/100,000/yr. (133.6 and 11.8, resp.). From 1961 to 1967, the frequency for males and females increased, with a greater increase for males. This was especially marked after age 55, with cancer of the prostate continuing to increase sharply, while cancer of the uterus and breast showed marked decreases. In 1965, Rumania was listed by the World Health Organization as number 25 of 43 nations arranged in increasing order of mortality due to neoplasms. Variations were seen for the different districts of Rumania, with doubtful explanations given. Only stomach cancer showed a significantly greater incidence in rural than in urban areas (20 and 23.5, resp.).

0-2516 MORBIDITY AND MORTALITY FROM CANCER IN THE TOWN OF BIRLAD AND THE FORMER DISTRICT OF BIRLAD FOR A PERIOD OF FIVE YEARS (1963-1967) IN URBAN, SUBURBAN AND RURAL REGIONS. (R.) Tască, C. V. (Birlad Gen. Hosp., Rumania). Oncol. Radiol. 8(5):451-456, 1970.

Annual morbidity and cancer mortality rates for a 5-yr. period (1963-1967, inclusive) are reported for a population of about 161,000 including 39,000 urban, 11,500 suburban and 110,500 rural inhabitants of the Birlad region in Rumania. In 1963, incidence and mortality rates from cancer were 123.2/100,000 and 74.3/100,000, resp. These values increased to 152.6/100,000 and 84.1/100,000, resp., in 1967. A gradual and constant increase was noted for all groups, with incidence and death rates highest in the urban areas, intermediate in suburban areas and lowest in rural areas. From 1963 to 1967, incidence of cancer increased from 128.1 to 155.0/100,000 for males and from 118.5 to 150.3/100,000 for females (entire region). Annual mortality rates increased from 85.0 to 87.5/100,000 for males and from 64.1 to 80.5/100,000 for females over the 5-yr. period. Further tabulations by site of cancer are presented.

70-2517 WORLD HEALTH STATISTICS REPORT. (E.) World Health Organization (Geneva, Switzerland). World Health Statistics Rep. 22(12):706-739, 1969.

Numbers of deaths from malignant neoplasms, according to site, sex and age recorded in urban areas of the USSR between 1958 and 1966, are tabulated on pages 726-737 of this report.

70-2518 CANCER DEATHS IN THE NEWBORN. (E.) Fraumeni, J. F., Jr. (NIH, Bethesda, Md.) and R. W. Miller. Amer. J. Dis. Child. 117(2):186-189, 1969.

Review of death certificates for all American children who died of malignant neoplasia under 28 days of age during 1960-1967 revealed 130 such deaths, for a death rate of 6.24/million live births. Teratomas, primary liver cancers and neuroblastomas were disproportionately frequent in relation to all cancer deaths under 5 yr. of age. Cancer deaths among the newborn showed an equal sex distribution, in contrast to a male preponderance in later childhood. Deaths did not cluster in time, space or families. Congenital defects were recorded in 12/130 cases. Down's syndrome was seen in 8/44 (18%) newborns who died of leukemia, a frequency much higher than that (1%) among older children.

70-2519 CANCER MORTALITY AMONG DIABETICS. (E.) Kessler, I. I. (Johns Hopkins U. Sch. Hyg. Public Health, Baltimore, Md.). J. Nat. Cancer Inst. 44(3):673-686, 1970.

Cancer mortality was determined among 21,447 Caucasian diabetics enrolled in a diabetes clinic in Massachusetts during the 26-yr. period, January, 1930-July, 1956. Total cancer mortality

among female diabetics occurred at about the expected frequency (544, with 530 expected). Male diabetics had a significantly reduced risk of cancer death (358, with 421 expected) that persisted even after exclusion of deaths from lung cancer. This decreased cancer risk was attributed to 2 factors: an especially excessive risk of death from causes other than cancer, and an over-representation of Jews among the diabetic pts. (17% of the diabetics were Jewish). Among the 15 specific types of cancer studied, a statistically significant excess in deaths was seen only for cancer of the pancreas. Diabetic females did not have an increased risk of death from cancer of the uterine corpus. Mortality from lung cancer was reduced significantly among male diabetics, but not among females. Diabetes preceded cancer in 98% of the males and 94% of the females.

70-2520 SOME CANCER PATTERNS IN WESTERN KENYA AND NORTH WEST TANZANIA. (E.) Burkitt, D. P., M. Bundschuh, K. Dahlin, L. Dahlin and R. Neale. *East Afr. Med. J.* 46(4):188-193, 1969.

Cancer records from 3 East African mission hospitals located at Kagondo, Ndolage (in northwest Tanzania) and Maseno (in western Kenya) were compared with each other and with previous reports from other similar hospitals. Data included frequency of cancer of the stomach and esophagus, Burkitt's lymphoma, Kaposi's sarcoma, and cancer of the cervix, penis and breast at Kagondo, Ndolage and Maseno. Cancer of the stomach was the most frequently reported neoplasm at both Kagondo and Ndolage hospitals, while at Maseno, esophageal cancer was the most frequent tumor. Burkitt's lymphoma was found only at Maseno. The findings emphasize the fact that significant differences in disease patterns can be detected over limited areas, with the resultant possibility of seeking the responsible environmental factors.

70-2521 CANCER AND AIR POLLUTION. ASPECTS OF GEORGRAPHICAL PATHOLOGY. (Fr.) Garbe, E. and M. Brunet. *Bull. Inst. Nat. Sante* 25(2):201-212, 1970.

Data on deaths from all cancers in France (both sexes) for 1961-1963 (inclusive), 1966 and 1967 were compared with data relating to air pollution levels, including consumption of petroleum and petroleum products, per capita consumption of fossil fuels, population density and the "urbanization coefficients" for each of the departements of France, obtained at various times from 1951 through 1966. Significant correlations were found between cancer death rates and parameters of air pollution, including a highly significant correlation between the 1961-1963 data on cancer deaths and the 1951-1953 data per capita fossil fuel consumption. A comparison of crude cancer mortality rates/100,000 population (av. for 1961-1963) and rates of petroleum consumption

per unit surface area (1951-1953) showed significant correlations between petroleum consumption and cancer of the larynx, lung and oral cavity in males, breast cancer in females and leukemia in both sexes. When the 1961-1963 data on lung cancer in males (used as an "index of urbanization") were compared with similar data for other tumor types in both sexes, the results suggested an urban predominance for cancer of the lung and the upper g.i. and respiratory tracts in males, breast and cervix cancer in females and leukemia in both sexes, and a rural predominance for cancer of the prostate, stomach and esophagus in males. The results suggest that industrialization and air pollution are not the only factors of importance in the epidemiology of cancer in urban areas.

70-2522 STATISTICAL RELATIONSHIP BETWEEN CANCER MORTALITY, MORTALITY FROM HEART DISEASE AND CERTAIN SOCIO-DEMOGRAPHIC FACTORS. (Fr.) Massé, H. *Bull. Inst. Nat. Sante* 25(2):295-306, 1970.

From 1960-1964 (inclusive), 94,049 deaths from malignant diseases (including leukemia) and 100,699 deaths from heart disease were reported in adults (both sexes) 45-64 yr. old in France. Crude and adjusted annual mortality rates/10,000 population (1960-1964 means) for cancer and heart disease, were tabulated separately for each of the 90 departements of France and for 4 occupational categories. Mortality rates for both cancer and heart disease were negatively correlated with occupation among farmers and among business and professional persons, and positively correlated with occupation among white-collar and blue-collar workers. These correlations were strong for both sexes, but were stronger in females than in males. It is suggested that better working conditions (such as less hazardous occupations for women) and better medical care might account for the differences between occupational groups in mortality from cancer and heart disease.

70-2523 THE PATTERN OF MALIGNANT DISEASE IN ILESHA, WESTERN NIGERIA. (E.) Mulligan, T. O. (Wesley Guild Hosp., Ilesha, Nigeria). *Brit. J. Cancer* 24(1):1-10, 1970.

In 1954-1967 (inclusive), 72,862 pts. were admitted to Wesley Guild Hospital, Ilesha, Nigeria including 465 pts. with suspected or histologically confirmed malignant tumors. The corrected crude annual incidence rate/100,000 population in Ilesha Township was 18.8 for all tumors combined (2.6 for carcinoma of the stomach; 1.5 for hepatoma; 1.3 for carcinoma of the cervix; 1.2 for reticulum cell sarcoma and lymphosarcoma; 1.6 each for Burkitt's lymphoma and abdominal tumors). These rates were lower than the rates for Ibadan and probably represent a gross underestimate of the number of cases. However, the age-specific incidence rates for carcinoma of

the stomach were about the same in this community in Ibadan and Connecticut.

2524 EPIDEMIOLOGY OF NEOPLASTIC DISEASES IN POLAND (BETWEEN 1965-1967). (Pol.)
 szarowski, T. (Oncol. Inst., Warsaw), H. Jodziejska, H. Gadomska, J. Staszewski, A. Wieczorkiewicz, Z. Karewicz and B. Warda. Pol. g. Lek. 25(12-13):440-443, 1970.

In all of Poland, the morbidity rates/100,000 population for all malignant tumors combined (1965-1967) were 115.4 in males and 127.0 in females. In Warsaw and Cracow, these rates were 179.0 and 179.1, resp., in males, and 264.7 and 267.8, resp., in females. In Katowice Province (which is both urban and rural), the rates were 148.2 in males and 147.2 in females. In 3 rural provinces (Minsk Maz. and Siedlce, Nowy Sacz and Cieszyn), the rates were 157.5, 132.1 and 184.9, resp., in males, and 157.9, 144.6 and 192.0, resp., in females. The most prevalent tumors in males, nationwide, were cancer of the stomach, lung, skin, lip and larynx (21.6%, 19.0%, 6.9%, 4.9% and 4.3% of all tumors, resp.); in females, the most prevalent tumors were cancer of the cervix, breast, stomach, skin and liver plus biliary tract (23.4%, 12.5%, 10.9%, 6.9% and 6.9% of all tumors, resp.). The most prevalent tumor among urban males (Warsaw and Cracow) was lung cancer, followed by stomach cancer; in rural males, the most prevalent tumor was stomach cancer, followed by lung cancer. In urban females, the most prevalent tumor was cervix cancer, followed by breast cancer; in rural females, the most prevalent tumor was stomach cancer, followed by breast cancer. The overall morbidity rates for lung cancer prevalence were lower in Katowice than in other cities. Liver and biliary cancer were more prevalent in Warsaw than in other areas. Cieszyn province showed the highest morbidity rate of all rural areas, and the highest frequency of rectal cancer. The predicted morbidity rates for 1985 are 207.9/100,000 in males and 217.7/100,000 in females.

2525 ANALYSIS OF THE INCIDENCE OF MALIGNANT TUMORS IN THE DISTRICT OF KATOWICE 1965. (Pol.) Staszewski, J. (Inst. Oncol., Katowice, Poland) and A. Wieczorkiewicz. Nowotwory 11(1):61-67, 1968.

In 1965, 4771 new cases of cancer (2116 in males, 2655 in females) were reported in the Katowice Province of Poland; the morbidity rates/100,000 population were 122.1 in males and 148.2 in females. The most prevalent tumors among males were cancer of the stomach, lung, skin, larynx and rectum (23.2%, 20.6%, 7.2%, 4.7% and 4.1% of all tumors in males, resp.). The most prevalent tumors in females were cancer of the cervix (including preinvasive lesions), breast, stomach, skin and liver plus bile ducts (24.9%, 13.2%, 11.6%, 4.1% and 6.2% of all tumors in females, resp.). Analysis of the age-specific morbidity rates

suggested an inadequate notification or diagnosis of malignant diseases among older persons in some areas. This hypothesis was reinforced by the fact that only 38% of the tumors in males and 57% of the tumors in females were confirmed histologically, with a particularly low histological confirmation rate for tumors of the internal organs. A wide variation in morbidity rates was noted among the 33 districts of Katowice province, with rates above 200/100,000 population in 2 districts (248 in Cieszyn and 210 in Czeszochowa); this geographical variation was attributed to differences in cancer detection and registration, rather than to inherent differences in morbidity.

70-2526 CANCER REGISTRATION IN ST. GALLEN/APPENZELL - EVALUATION FOR 1960-1968.

(Ger.) Brändli, O. (Canton Hosp. Path. Inst., St. Gallen, Switzerland). Z. Praev.-Med. 14(6):371-392, 1969.

From June 1, 1960-December 31, 1968, 7313 new cancers (3390 in males, 3923 in females), confirmed histologically (biopsy or autopsy), were reported among residents of the cantons of St. Gallen and Appenzell. Crude annual morbidity rates/100,000, for all tumors except skin cancer and leukemia, were 189 in males and 207 in females (increasing from 186 and 198, resp., in 1961-1964 to 199 and 215, resp., in 1965-1968). When leukemia and skin cancer were added, the crude annual morbidity rate for both sexes was somewhat over 300/100,000. Comparison of the 1961-1967 data on cancer registration and cancer deaths indicated that only about 65% of all tumors (70% in males, 55% in females) were registered; this relatively low registration rate was believed to explain why these morbidity rates were lower than those previously reported for Norway (1957-1961), Denmark (1953-1957) and Connecticut (1960-1962). Multiple tumors were found in 2.2% of the total group (161 pts.). During the study period, the most prevalent tumors in males were cancer of the lung, stomach, prostate, large intestine, rectum and oral cavity (crude annual morbidity rates/100,000 were 29, 25, 22, 12, 11 and 11, resp.); in females, the most prevalent tumors were cancer of the breast, uterus, stomach, cervix (excluding carcinoma in situ) and ovary (crude annual morbidity rates/100,000 were 52, 21, 19, 17 and 16, resp.). From 1961-1964 to 1965-1968, uterine cancer increased 23% (by 40%, when preinvasive cervix cancers were added). In both sexes, the rates for lung cancer and large intestine cancer increased (by 29% and 35%, resp.), while the rate for stomach cancer declined in both sexes, especially in females (by 32%).

70-2527 NAEVUS SEBACEUS. A REPORT OF 140 CASES WITH SPECIAL REGARD TO THE DEVELOPMENT OF SECONDARY MALIGNANT TUMOURS. (E.) Jones, E. W. (St. John's Hosp. Inst.

Derm., London) and T. Heyl. *Brit. J. Derm.* 82(2):99-117, 1970.

This series of 140 pts. (seen in 1956-1957) included 5 children aged 0-9 yr., 52 pts. aged 10-19 yr. and 34 pts. aged 20-29 yr. Most of the tumors involved the head and neck, especially the scalp. Associated tumors included syringocystadenoma papilliferum in 27/140 (with areas of basaloid proliferation in 7/27), basal cell carcinomas in 9 pts. (only 3/9 seemed to be aggressive), benign basaloid proliferations in 14 pts., 3 syringomas, 2 apocrine cystadenomas, 2 osteomas, 1 rare case of poorly differentiated squamous cell carcinoma, and other types of unusual squamous cell proliferation in several other pts. None of these tumors recurred after surgery. It is concluded that the risk of a serious malignant tumor supervening in a nevus sebaceus is small and that simple surgical excision is adequate.

70-2528 SECULAR TRENDS IN MORTALITY FROM MALIGNANT MELANOMA. (E.) Lee, J. A. H. (U. Washington, Seattle) and A. P. Carter. *J. Nat. Cancer Inst.* 45(1): 91-97, 1970.

Death rates from malignant melanoma in the U.S. were higher in all age groups in 1967 than in 1960. In England and Wales, while the death rates from malignant melanoma increased at all ages from 1951-55 to 1961-65, the increase was proportionately greatest in middle age. Trends in age-specific mortality rates are compatible with a generation effect, beginning with those born around 1900. The current increase in the death rate from malignant melanoma is more likely due to an increased incidence of the disease than to a simple improvement in death certification (prior to 1950, deaths from malignant melanoma were included under those from skin malignancies).

70-2529 ANALYSIS OF ETIOLOGICAL FACTORS OF SQUAMOUS CELL SKIN CANCER OF DIFFERENT LOCATIONS. 2. THE TRUNK AND HEAD. (E.) Hillström, L. and G. Swanbeck (Karolinska Inst., Stockholm). *Acta Dermatovener. (Stockholm)* 50(2):129-133, 1970.

From 1958-1966 (inclusive), 100 cases of squamous cell skin carcinoma of the trunk (59 males, 41 females) were reported to the Swedish Cancer Registry. Associated factors in 22 pts. included fistulas (4 pts), burn scars, mechanical injuries, psoriasis, eczema, other skin diseases and X-ray treatment (3 pts. each). In addition, 3724 squamous cell carcinomas of the head were reported in 1958-1967, comprising (about 80% of all squamous cell skin cancers). Frequencies of squamous cell carcinoma of the facial skin were about the same in males and females, with the exception of cancers of the external ear, 90% of which were found in males (apparently because of greater exposure of the ears to

sunlight in males than in females). Squamous cell carcinomas of the skin of the head were more frequent (relative to total population) in the southern part of Sweden than in the northern regions.

70-2530 CELLULAR TYPES, SURVIVAL, RACE, NATIVITY, OCCUPATIONS, HABITS AND ASSOCIATED DISEASES IN THE PATHOGENESIS OF LIP CANCERS. (E.) Keller, A. Z. (VA Cent. Office, Washington, D. C.). *Amer. J. Epidemiol.* 91(5):486-499, 1970.

The study group included 314 men with carcinomas of the lip and 2 control groups of equal size (men with carcinomas of the oral and pharyngeal mucous membranes, and men with other diseases), comprising a 20% sample of all males discharged from VA hospitals throughout the U.S. during 1958-1962. The group of pts. with lip cancer included 3 Negro men (1.0%; compared to 12.8% of the general control group). For the 311 white pts., the annual prevalence rate/100,000 living male veterans (as of 1960) was 1.57. Less than 5% of the 294 squamous cell carcinomas, but 9/16 basal cell carcinomas, involved the upper lip. All 31 tumors which had metastasized (30 squamous cell and 1 basal cell) involved the lower lip. Among the white pts., lip cancer was significantly associated with native residence in the South or emigration from the South to the Rocky Mountain region (especially Arizona and New Mexico); with pipe, cigar and cigarette smoking (although no significant association between lip cancer and pipe smoking alone was found); and with outdoor occupations such as farming. Lip cancers were also strongly associated with cancers of the environmentally-exposed skin (head, face and neck). The lip cancer risk increased with age, but lip cancer was not an important contributor to the causes of death.

70-2531 ORAL AND PHARYNGEAL CANCER IN MADHYA PRADESH. (E.) Gandagule, V. N. (Med. Coll., Jabalpur, India) and S. Agarwal. *J. Indian Med. Ass.* 53(12):582-585, 1969.

In Madhya Pradesh, India during the period 1958-1967, there were 814 cases of oral and pharyngeal squamous cell carcinoma which were analyzed according to incidence, site, age, sex, community and histologic features. These 814 cases accounted for 33.8% of all malignancies (48% in males and 18% in females). Estimated incidence rose steeply with age. The av. age for hypopharyngeal cancer (52.8 yr.) was slightly higher than for oral and oropharyngeal cancer (48.9 yr.). Males comprised 72.2% of the cases, females only 27.8%. In the population at risk, Hindus comprised 93.0% and Mohammedans 5.0% of the local population. For both males and females, the incidence of oral and pharyngeal carcinoma was higher in Mohammedans compared to Hindu population; this

as attributed to the habit of chewing tobacco. The distribution of oral, oropharyngeal and hypopharyngeal cancer was 63.1%, 20.1% and 16.8%, resp. The buccal mucosa, the base of the tongue and the pyriform sinus were the most commonly affected sites in the oral cavity, oropharynx and hypopharynx, resp.

0-2532 THE PATHOLOGY OF ORAL CANCER IN PAPUA AND NEW GUINEA. (E.) Cooke, R. A. Roy. Brisbane Hosp., Australia). Papua N. Guinea Med. J. 12(3):84-90, 1969.

A total of 490/3085 (15.8%) cancers seen in Papua and New Guinea in 1958-1967 (inclusive) included 47 cancers of the lip, 96 of the tongue and 347 of the buccal mucosa and floor of mouth (1.6%, 19.6% and 70.8%, resp.), with a male:female ratio of 2.7:1. Examination of 42 cases of buccal mucosa carcinoma and 9 cases of tongue carcinoma revealed lymph node metastases in 14/42 and 5/9, resp. Buccal cancers (90%) were all differentiated and all cases of tongue and lip cancers were also well differentiated. The size of the tumors of the buccal mucosa and tongue was related to presence or absence of lymph node metastases. Lymph node metastases were not found in any of the pts. with lip cancer. Early all cases of oral cancer were from the coastal areas where chewing betel nut is common.

0-2533 CARCINOMA OF THE OESOPHAGUS. COMPARISON OF TWO RADIOLOGICAL SERIES FROM JAMAICA AND WESTERN AUSTRALIA. (E.) Bateson, M. (Univ. Hosp. West Indies, Mona, Kingston, Jamaica). Aust. Radiol. 13(4):345-349, 1969.

A radiological series of carcinoma of the esophagus from Kingston, Jamaica (during 1962-1967; 7 cases) and Perth, Western Australia (1960-1965; 72 cases) were compared. Western Australia has a population predominantly Caucasian in origin, living in good social and economic conditions, on a good diet, while Jamaica has a population predominantly of African origin, living in very poor social and economic conditions, on a poor or deficient diet. The variety of alcohol consumed in the 2 areas is also different (beer in Australia and rum in Jamaica). Despite these differences, the age distribution, sex ratio, anatomical distribution and extent of involvement of the esophagus were very similar in these 2 series. In Jamaica the male:female ratio was 1.7:1, while in Western Australia it was 2.6:1. The peak prevalence in both areas was between 60-69 yr. of age. It is suggested that the behavior of esophageal carcinoma was not modified by differences in environment or race in these 2 areas.

0-2534 EPIDEMIOLOGY OF LARYNGEAL CANCER IN THE KIROVOGRAD REGION FOR THE 10 YEARS, 1958-1967. (Rus.) Samokhodskii, V. N. (Kirovograd Oncol. Dispens., USSR). Zh. Ushn. Nos. Bol. 30(1):74-78, 1970.

In the Kirovograd region in the south-central Ukraine, 224 cases of laryngeal cancer were reported between 1958 and 1967. Laryngeal cancer accounted for 0.9% of all cancers and for 55.5% of all upper respiratory cancers. Both the crude and age-standardized incidences of laryngeal cancer increased almost double between 1958-1962 and 1963-1967. For men, the age-standardized incidence increased from 2.81/100,000 to 5.73/100,000. The increase was larger among urban males (from 1.23 to 3.69/100,000) than among males living in rural areas (from 1.18 to 1.64/100,000). No cases of laryngeal cancer were reported in females between 1958 and 1962. From 1963 to 1967 the age-standardized incidence for women was 0.48/100,000 in urban areas and 0.09/100,000 in rural areas. The ratio of male to female cases in the entire region was 100:11. When analyzed by social class the age-standardized incidences were highest among the unemployed (1.08/100,000) and lowest (0.3/100,000) among collective farmers. Geographically, laryngeal cancer occurred most frequently in the south-eastern steppes (1.06/100,000) and in the central area where most of the urban dwellers live (0.93/100,000). These incidences for laryngeal cancer in the Kirovograd region were significantly higher than figures previously established for the Western Ukraine (Rovno and Volyn regions), Kirghizia, and Uzbekistan but were lower than those for the USSR as a whole. The most common histological form of laryngeal cancer was keratinized squamous cell carcinoma (43.1%) followed by nonkeratinized squamous cell carcinoma (30.5%).

40-2535 SMOKING, AIR POLLUTION, AND BRONCHITIS IN BRITAIN. (E.) Lambert, P. M. (Gen. Register Office, London W.C.2) and D. D. Reid. Lancet 1(7652):853-857, 1970.

A survey of the prevalence of respiratory symptoms in England, Wales and Scotland was conducted in 1965, eliciting replies from 9975 men and women aged 35-69 yr. Respiratory symptoms increased in relation to both age and cigarette consumption. A male excess was noted in both smokers and nonsmokers. Prevalence rates increased with increasing rates of air pollution; this increase was independent of cigarette consumption. Local air pollution had little effect without cigarette smoking, but high pollution levels were associated with a high prevalence of respiratory symptoms in smokers. The sharpest increase with age in the frequency of serious bronchitis was seen among smokers in areas of highest air pollution.

70-2536 RECENT TRENDS IN MORTALITY FROM LUNG CANCER AND BRONCHITIS IN URBAN AND RURAL AREAS IN SCOTLAND. (E.) Crofton, E. C. (U. Edinburgh). Brit. J. Prev. Soc. Dis. 24(2):110-115, 1970.

Age-standardized and age-specific mortality rates from respiratory tumors and bronchitis in males were calculated for urban and rural areas of Scotland for 1951-1965. The standardized mortality rates for both diseases, and every age-specific death rate except those for the 45-54-yr. age group in the cities, increased steadily during this period. For each age group, the ratio between death rates in cities to death rates in rural areas decreased during this time; the greatest decrease in ratio for lung cancer occurred in the 55-64-yr. age group and for bronchitis in the 45-54-yr. age group. Population movements, changes in air pollution and differences in diagnosis and treatment apparently did not have a major role in the changing relationships between urban and rural death rates. It is suggested that a later beginning and subsequent marked increase in cigarette smoking in the rural areas could account for many of the changes observed.

- 70-2537 ENVIRONMENTAL FACTORS IN THE AETIOLOGY OF LUNG CANCER AND BRONCHITIS. (E.) Gardner, M. J. (London Sch. Hyg. Trop. Med.) and R. E. Waller. *Brit. J. Prev. Soc. Med.* 24(1): 58-60, 1970.

Sources of error in studies of the relationship between lung cancer mortality and air pollution are discussed. Particular reference is made to Ashley's use of "modified Standardized Mortality Ratios" (SMR) for communities of different populations and degrees of urbanization. Use of modified SMR reduces the association between mortality rates and factors such as air pollution and population density, which are related to the size of the community. Objections are also registered to the use of air-pollution data collected from districts of less than the highest population density, and to collection of data on smoke and sulfur dioxide pollution limited to short periods of time (a 1-yr. collection period is advised).

- 70-2538 EPIDEMIOLOGICAL STUDY OF LUNG CANCER WITH SPECIAL REFERENCE TO THE EFFECT OF AIR POLLUTION AND SMOKING HABITS. (E.) Hitosugi, M. (Nat. Cancer Ctr. Res. Inst., Tokyo). *Koshu-Eisei-in-Kenkyu-Hokoku (Bull. Inst. Publ. Hlth.)* 17(3):237-256, 1968.

Relationships between air pollution, cigarette smoking and cancer of the lung were studied in 1965 in 2 adjacent cities near Osaka, Amagasaki (a highly-industrialized city with relatively high air pollution) and Nishionomiya (a residential area) were classified into 3 areas of high, intermediate and low air pollution. Detailed smoking histories were obtained for lung cancer cases (deaths over a 7-yr. period, 1960-1966) and for a random sample of adults from both cities. Death rates/100,000 population (aged 35-74 yr.) were significantly higher in the

high-air pollution areas than in areas of intermediate and low pollution for males (27.6, 17.2 and 17.7, resp.) but not for females (7.5, 9.8 and 7.2, resp.). Lung cancer death rates were higher in smokers than in nonsmokers for both sexes. A cross-tabulation between the levels of air pollution and cigarette consumption showed a significantly higher death rate among smokers than among nonsmokers at each level of air pollution. Lung cancer death rates increased slightly in proportion to the amount of air pollution in smokers, but not in nonsmokers. The possibility of a synergistic action between smoking and air pollution is discussed.

- 70-2539 LUNG CANCER AMONG THE JEWS. (E.) Horowitz, I. (McGill U., Montreal, Quebec, Canada) and P. E. Enterline. *Amer. J. Public Health* 60(2):275-282, 1970.

In 1956-1966, 284 males and 76 females from an economically homogenous area of Montreal (with a population about equally divided between Catholics, Jews and other religious groups), died with lung cancer. Age-adjusted mean annual lung cancer death rates/100,000 population during this period among Catholics, Protestants and Jews, were 36.0, 32.4 and 21.5, resp., in males, and 5.0, 6.6 and 9.2, resp., in females. In persons of French, British, Jewish and other origins, these rates were 27.8, 41.1, 22.0 and 26.4, resp., in males, and 5.5, 5.5, 9.7 and 5.8, resp., in females. It is suggested that the rate among males of British origin may be due to an extremely high death rate among Catholic males of British origin. Studies of tumor histology and smoking habits suggested that the high rate among British males and the low rate among Jewish males could be explained by differences in smoking habits. The high rate in Jewish females, however, could not be entirely explained by smoking behavior.

- 70-2540 LUNG CANCER AMONG THE JEWS AND NON-JEWS OF PITTSBURGH, PENNSYLVANIA, 1953-1967: MORTALITY RATES AND CIGARETTE SMOKING BEHAVIOR. (E.) Herman, B. (U. Texas Med. Branch, Galveston) and P. E. Enterline. *Amer. J. Epidemiol.* 91(4):355-367, 1970.

In 1953-1967 (inclusive), lung cancer was recorded as the underlying cause of death for 458 white men and 114 white women aged 45 and over, residing in an economically homogeneous area of Pittsburgh. The av. annual age-adjusted death rates from lung cancer/100,000 population in this age group were 92.5 for male Jews, 148.6 for male non-Jews, 41.8 for female Jews and 21.7 for female non-Jews. Studies of the proportions of various histological types of lung cancer and a survey of smoking habits among the cancer pts. suggested that the low lung cancer rate among Jewish males could be explained by a relatively low rate of cigarette smoking.

a relatively high rate among Jewish females, however, could not be entirely explained by smoking behavior. The possible effects of differences in diagnosis and reporting, biological and genetic factors, and frequencies of metastatic adenocarcinomas of the lung are discussed in an attempt to explain these findings.

- 2541 CARCINOMA OF THE LUNG IN WOMEN. (E.) Deaner, R. M. (Naval Hosp., San Diego, Calif.) and M. J. Trummer. J. Thorac. Cardiovasc. Surg. 59(4):551-554, 1970.

Primary carcinoma of the lung was confirmed in women from 1962-1967, inclusive, treated at the San Diego Naval Hospital. In comparison, there were 324 males with primary bronchogenic carcinoma (the male:female ratio was 4.7:1). The tumors in women were classified as undifferentiated carcinomas (60%), adenocarcinomas (27%) and epidermoid carcinomas (13%). It is concluded that the epidermoid and undifferentiated carcinomas are more associated with heavy cigarette smoking, than the adenocarcinomas. Figures associated with operability, diagnosis, management and survival indicate no differences between men and women pts.

- 2542 CANCER OF THE LUNG IN NATAL BANTU - A NEW CANCER PROBLEM. A REVIEW OF 472 CASES, 1964-1966. (E.) Schonland, M. (U. Natal, Durban) and E. Bradshaw. S. Afr. Med. J. (34):1058-1060, 1969.

Analysis of 472 cases of lung cancer among Natal Bantu registered during 1964-1966 revealed that lung cancer caused 17.7% of all Bantu male cancers, but only 2.9% of all Bantu female cancers in Natal province, South Africa. Over a 12-yr. period, the yearly av. of lung cancer increased 3-fold among Bantu males and 2-fold among Bantu females. The geographical distribution of lung cancer in the Bantu population was well correlated with the distribution of the Caucasian population in Natal, being higher where there were more Caucasians. There appeared to be an association between lung cancer and economic opportunities and western influences which may promote cigarette smoking. Age distribution showed that 72.2% of all male cases occurred between the ages of 40 and 64 yr., while the frequency of female cases rose steadily with age. It is suggested that methods be introduced among Bantu males 30-60 yr. of age to promote early detection and to reduce cigarette smoking.

- 2543 BRONCHIAL CARCINOMA IN EAST GERMANY. (Ger.) Römer, K.-H. (Med. Acad. Magdeburg Surg. Clin., Germany). Z. Aerztl. Fortbild. (Jena) 63(15):805-809, 1969.

A 50% increase in the number of cases of bronchial carcinoma was seen in East Germany

between 1953-1965. In 1965, 39,624/230,254 (17.2%) deaths were due to malignancy. Bronchial carcinoma, causing 16% of all cancer deaths, was the second most frequent cause of death from cancer (after stomach cancer, with 21%) in East Germany. In 1965, a total of 5650 men and 726 women died of cancer of the lungs and bronchi (28.4% of all male and 3.7% of all female cancer pts.). The peak morbidity and mortality was seen between 65-75 yr. for males and 70-75 yr. for females (0.9% of the male and 2.7% of the female pts. were less than 40 yr. old). Mortality differed in different provinces and was markedly higher in industrial and congested areas. In 1964, mortality from bronchial carcinoma in East Germany was 32.2/100,000 (as compared to 89.5/100,000 in England and 30.4/100,000 in France). The carcinogenic significance of smoking (80-96% were heavy smokers) and exposure to environmental carcinogens are briefly mentioned, and the importance of early diagnosis and surgical treatment are discussed.

- 70-2544 SYNTHETIC SWEETENER CONSUMPTION AND BLADDER CANCER TRENDS IN THE UNITED STATES. (E.) Burbank, F. (NCI, Bethesda, Md.) and J. F. Fraumeni, Jr. Nature (London) 227(5255):296-297, 1970.

In a study of the general use of cyclamates and the toxicity of artificial sweeteners, the U.S. Department of Health, Education and Welfare found no clear-cut separation in age-specific or age-adjusted mortality rates for bladder cancer from 1950-1967, inclusive (1962 being the yr. cyclamate consumption dramatically increased). Incidence rates for bladder cancer showed only a long-term increase in rate (by about 8/100,000 over the 17-yr. period) which may be related to cigarette smoking. As yet, bladder cancer rates do not appear affected by synthetic sweeteners, but the time period is considered too short and the dosage too low for examples of cyclamate carcinogenicity to have appeared. Chromosome breaks in vivo in rats and in vitro in human cells due to cyclamates and cyclohexylamine are also mentioned.

- 70-2545 PHENACETIN-CONTAINING DRUGS AND CARCINOMA OF THE URINARY TRACT. (Sw.) Angervall, L. (Sahlgrenska Hosp., Goteborg, Sweden), U. Bengtsson, S. Johansson and L. Wahlqvist. Lakartidningen 66(44):4525-4532, 1969.

In Sweden, a 5-yr. study of a group of pts. with a long history of phenacetin abuse (1 g or more/day) showed that about 8% developed renal pelvic carcinoma, a relatively rare disease. From 1960-1966 an av. of 41 cases/yr. were diagnosed for the general Swedish population (1:183,00 inhabitants). In comparison, previously mentioned studies showed 9 cases in 9 yr. in the city of Gothenburg and 9 cases in 9 yr. at the

nearby Huskvarna weapons factory, where phenacetin abuse among employees was notoriously high. Carcinoma of the bladder also developed in some pts.

70-2546 REGIONAL DIFFERENCES IN DEATH FROM GASTRIC CANCER IN OSAKA AND NARA PREFECTURES. (Jap.) Mega, T. (Nara Med. U., Japan), S. Tomii, T. Yoshida and H. Arachi. Nara Igaku Zasshi (J. Nara Med. Ass., 19(2): 270-272, 1968.

In Nara Prefecture, stomach cancer mortality rates were the highest in Japan; Osaka Prefecture contained 3 regions of high mortality rate. Age-adjusted stomach cancer death rates for all of Japan (1962) were 5.7/10,000 in males and 3.5/10,000 in females. In 4 high-stomach cancer districts (1960-1964), these rates were 8.0-12.4/10,000 in males and 4.2-8.1/10,000 in females. On both sides of the common border of the Nara and Osaka prefectures (the Katsuragi Mountains), mortality rates were high in the northern area of farm villages, and low in the southern area of mountain villages.

70-2547 EPIDEMIOLOGY OF STOMACH CANCER IN UZBEKISTAN. (Rus.) Statnikov, A. M. (Uzbek Sci. Res. Inst. Roentgen. Radiol. Oncol., USSR) and K. G. Bobrina. Med. Zh. Uzbek. (5):48-50, 1969.

In Uzbekistan the age-adjusted incidence of stomach cancer was 27.3/100,000 and 12.4/100,000 inhabitants for men and women, resp., in 1962-1963. In an unspecified yr., 34.1% of all pts. who died of cancer in Uzbekistan died of stomach cancer. This republic ranked number 8 in the USSR for incidence of stomach cancer in men and number 11 for women. The number of cases of stomach cancer diagnosed in Uzbekistan increased from 966 in 1961 to 1954 in 1964 due to diagnostic improvements, expansion of medical facilities, an increase in number of cancer specialists and improvements in their training. The incidence of stomach cancer differed among the various ethnic groups and among the different geographical regions in Uzbekistan. Stomach cancer was almost 4-fold as common in Russians and Ukrainians as in Uzbeks and more than 5-fold as common among Kara-Kalpaks; this is attributed to differences in living habits, customs and dietary habits. Stomach cancer was most prevalent in the city of Tashkent and the Fergana and Samarkand regions, and was least prevalent in the Khoresm, Bukhara and Syr Darya regions. These differences are largely explained by the fact that the Russian and Ukrainian population of Tashkent is much larger than that of other parts of the republic.

70-2548 FEATURES OF THE COURSE OF STOMACH CANCER UNDER CONDITIONS PREVAILING IN

THE YAKUT ASSR. (Rus.) Krivoschapkin, V. G. (Yakutsk U., USSR). Ter. Arkh. 42(1):54-57, 1970.

Between 1965 and 1968, the frequency of stomach cancer in Yakutia was 45/100,000. This is considerably higher than frequencies in other parts of the USSR (Ukraine 26.7, Belorussia 28.1, Uzbekistan 12.1, and Kazakhstan 16.3/100,000). In the Far north of Yakutia the frequency of this form of cancer was even higher (109/100,000) despite the fact that the diagnostic facilities in this area are poor and few autopsies are performed. The frequency of stomach cancer was 2.5-fold higher among indigenous Yakutians than among newcomers. Of 33 pts. with stomach cancer (20 Yakuts, 4 Russians, and 9 from other regions of the USSR), 17 had histories of gastritis and 5 of ulcer symptoms dating back 3-20 yr. or more, while 11 had no history of digestive disorders until immediately before stomach cancer was diagnosed. Among pts. with long histories of g.i. disorders, gastritis or ulcers might be considered precancerous, but sudden and imperceptible development of cancer could not be ruled out. These findings suggest that the high frequency of stomach cancer in Yakutia is due to the relatively large percentage of pts. with no histories of g.i. disorders.

70-2549 STOMACH CANCER IN YUGOSLAVIA: MORTALITY STATISTICS FROM 1961 TO 1966. (Ser.) Krajinović, S. (U. Belgrade Inst. Epidemiol., Yugoslavia) and S. Dutsić. Srpski Arh. Celok. Lek. 97(10):1011-1018, 1969.

An analysis of Yugoslavian mortality statistics showed that although the total cancer mortality increased from 80.9/100,000 in 1961 to 86.6/100,000 in 1966, the mortality for stomach cancer remained essentially unchanged during this period (15.59-16.23/100,000). This contrasts with findings from the U.S., Norway and the Netherlands, where stomach cancer mortalities have decreased. During the period studied, stomach cancer accounted for 18.63-20.47% of all cancer deaths in Yugoslavia. The age-adjusted death rates were higher among men (18.58-19.24/100,000) than among women (12.77-13.37/100,000); the male:female ratio was 1.4-1.5:1. The risk of dying of stomach cancer was low in the under-45 yr. age groups and reached a max. at 65-75 yr., after which it decreased. After age 45, the risk of dying of stomach cancer was higher among men than women of the same age. Great regional variation in stomach cancer death rates was seen. Rates were highest in Slovenia (34.86/100,000) and Croatia (26.09/100,000) and lowest in Bosnia and Herzegovina (5.33/100,000) and Montenegro (6.14/100,000). These regional variations may reflect differences in health care facilities, in practices used to record the cause of death, and in age structure of the population, as well as in environmental factors.

50 POPULATION STUDIES IN PATIENTS WITH GASTRIC CANCER. (E.) Oszacki, J. (Oncol. Cracow, Poland), H. Nosek and M. (Polk. Acta Med. Pol. 9(4):427-429, 1968.

g 1952-1966 in Cracow, Poland, 1561 (53%) 39 pts. with stomach cancer seen in an out-patient department, were treated surgically. Age of pts. was 53.7 yr., and the male:female ratio was 2:1. Among 687 resected cases, metastases to lymph nodes were found in 65.9%. Group analysis among those with stomach cancer revealed that 42.5% were of type A; 22.8%, type B, 0; and 7.8%, AB while for the general population of Cracow, blood types were 39.2%, 32.5% and 8.2%, resp. Among pts. with stomach cancer, 30.6% were born during the first half of the yr.

51 THE RELATIONSHIP BETWEEN PERNICIOUS ANEMIA AND CANCER OF THE STOMACH. (E.) Hoffman, N. R. (Hennepin County Gen. Hosp., Minneapolis, Minn.). Geriatrics 25(4):90-95, 1970.

Study of 138 pts. (mean age at diagnosis was 65 yr.) with pernicious anemia at Hennepin County Hospital, Minneapolis from 1960-1968 showed 7 preexisting malignancies involving the blood, stomach, colon and bone marrow. Other disorders included diabetes mellitus, hypothyroidism and gastric polyps. Since no cases of gastric carcinoma were diagnosed despite a mean follow-up of 11 yr., and since the incidence of stomach cancer has declined while the reported incidence of pernicious anemia has remained constant, it is suggested that there is no relationship between pernicious anemia and development of stomach cancer.

52 CANCER OF THE STOMACH IN UTAH - AN ANALYSIS OF 637 CASES. (E.) Dixon, J. C. R. Smart and V. Moslander. Rocky Mtn. Med. J. 67(4):47-50, 1970.

Study of 637 cases of stomach cancer reported in the Utah State Tumor Registry during the period January, 1957-July, 1969 was reviewed. Mean age of pts. was 64.5 yr. (387 men, 260 women). There were only 2 Negroes and 3 non-white pts. in the group. A rather uniform distribution of cases was seen throughout the state except for Carbon County, which had 25 histologically-proven cases of stomach cancer. Carbon County is predominantly a soft coal mining area and borders on the uranium mining region. In 1969, Carbon County had a population of 17,000 and reported 9 cases of stomach cancer, whereas the rest of the county, with a population of 130,000, had 10 cases in the same yr. Ethnic background did not explain the increased incidence in Carbon County, since it has a rather heterogeneous population. At time of report, a detailed epidemiological study of the pts. from

this county was being undertaken by the Tumor Registry.

70-2553 PRIMARY MALIGNANT TUMORS OF THE SMALL INTESTINE. (E.) Reyes, E. L. and R. W. Talley (Henry Ford Hosp., Detroit, Mich.). Amer. J. Gastroent. 54(1):30-43, 1970.

For the period 1953-1968, of all 65 cases (62 pts.; 41 men, 21 women, 25-80-yr.-old) of primary malignant tumors of the small intestine (0.26% of all malignancies recorded) presenting at Henry Ford hospital, Detroit, the greatest number was in the 50-70-yr. age group. Adenocarcinoma was the most common (38.4%) and occurred most often in the duodenum (12/25 cases). The jejunum had 80% of the leiomyosarcomas. Carcinoid tumors were found in 18 cases (27.7%). The duodenum, jejunum, and ileum contained 23%, 37% and 40% of all tumors, resp. Survival was correlated best with the stage of disease at diagnosis; pts. with lymphomas and ileal neoplasms survived longest.

70-2554 PRIMARY CARCINOMA OF THE JEJUNO-ILEUM IN JAPAN. (Jap.) Kurakane, K. (Kanazawa U. Cancer Res. Inst., Japan) and K. Morinaga. Ann. Rep. Cancer Res. Inst. Kanazawa Univ. 3(2):266-274, 1970.

The Japanese medical literature since 1912 disclosed 155 cases of carcinoma of the jejunum (96 pts.), ileum (33 pts.) or Meckel's diverticulum (2 pts.). The male:female ratio in this group was 1.8:1; the age range was 16-77 yr. (av., 54.8 yr.). The number of reported cases increased sharply in the 15-yr. period beginning in 1956.

70-2555 CARCINOMA OF THE COLON, RECTUM, AND ANUS. (E.) Franklin, R. (Vanderbilt U. Sch. Med., Nashville, Tenn.) and B. McSwain. Ann. Surg. 171(6):811-818, 1970.

From 1925-1968, 1022 pts. underwent surgery at Vanderbilt University Hospital for cancer of the colon, rectum and anus. Carcinomas of the colon comprised 45.4% of the large intestinal tumors seen in 1925-1948, compared to 76.8% in 1961-1968; the relative frequency of colon carcinomas increased from 1:737 hospital admissions in 1925-1948, to 1:369 admissions in 1961-1968. The ratio of Caucasian to Negro pts. with large intestinal cancer corresponded to the ratio seen among all pts. admitted, throughout this period. No difference in sex distribution was seen for the 1925-60 period and among pts. with carcinoma of the rectum and anus for 1961-8, but in the later period, only 99 men (compared to 141 women) had carcinoma elsewhere in the large intestine. In 1925-60, polyps were present in 7% of carcinoma pts. as compared to 24.4% in 1961-8.

- 70-2556 PREVALENCE OF UNDIAGNOSED CANCER OF THE LARGE BOWEL FOUND AT AUTOPSY IN DIFFERENT RACES. (E.) Berg, J. W. (NCI, Bethesda, Md.), A. Downing and R. J. Lukes. *Cancer* 25(5):1076-1080, 1970.

Records of the Los Angeles County Hospital for 1953-1959 (inclusive), comprising 16,105 autopsies, were studied. Undiagnosed bowel cancers were classified as asymptomatic (latent) and symptomatic. The prevalence of undiagnosed cancer of the colon and rectum was higher in women than in men; 77/132 tumors in females and 70/228 in males were undiagnosed. Undiagnosed cancer was less prevalent in Negroes (12/37) and much less prevalent in Mexicans (2/14) than in Caucasians (130/406) or Orientals (1/2). In this pt. group, 18% of the symptomatic cancers were not diagnosed before death (the primary reasons for a failure of diagnoses were poor condition upon admission and the presence or history of another disease, such as stomach cancer or cirrhosis, which could have caused the symptoms observed). In contrast to latent cancer of other sites, latent colon cancer resembled clinical colon cancer epidemiologically (i.e., order of magnitude of prevalence, site and sex distribution). Cancer of the rectum remained undetected much less often than cancer of the colon.

- 70-2557 COLORECTAL CANCERS IN JAMAICA: A REVIEW (1958-1967). (E.) Gilmour, J. *Dis. Colon Rectum* 12(5):357-363, 1969.

Cases of colorectal cancer treated in Kingston, Jamaica, Hospitals during the 10-yr.-period 1958-1967 were studied, with data derived mainly from the University Hospital. The ratio of females to males was 3:2; in the 1960 census, the sex ratio in Kingston was 6:5; more women had colorectal cancer than could be accounted for by their larger number in the population. In men, g.i. cancers were more common in the upper part of the g.i. tract than in the large intestine, while in females the distribution was about equal. Peak incidence of colorectal cancer in Jamaica occurred in the 50-70 yr. age group, with equal distribution in the 2 decades. Incidence by site of cancers at University Hospital showed that there were equal numbers (114) of cancers in the colon, rectal and anal regions. In Jamaica, colorectal cancer was twice as common as lung cancer. Operability, mortality rates, grading, survival time and recurrence rates are also discussed.

- 70-2558 COLONIC CANCER ARISING IN POLYPOSIS COLI. (E.) Ashley, D. J. B. (Morrison Hosp., Swansea, Wales). *J. Med. Genet.* 6(4):376-378, 1969.

Reanalysis of the work of Veale (1965) on the age-dependence of cancer in polyposis coli revealed that in pts. carrying the polyposis gene

the prevalence of colonic cancer at age 50 was 825,000/million in males and 830,000/million in females compared to 1335 and 1735/million, resp., in the general population (Doll et al. 1966). By age 70 the prevalence of colonic cancer in polyposis pts. was almost 100%, in contrast to 1/1000 in the general population. It is suggested that the effect of the polyposis gene is to reduce the number of changes necessary in the intestinal mucosal cells before neoplasia can develop, but that the development of cancer in the polyps is dependent on the same external factors as those in colonic cancer not preceded by polyposis.

- 70-2559 PRIMARY CARCINOMA OF THE LIVER IN HIROSHIMA AND NAGASAKI, JAPAN. (E.) Schreiber, W. M. (Atomic Bomb Casualty Comm., Hiroshima, Japan), H. Kato and J. D. Robertson. *Cancer* 26(1):69-75, 1970.

As based on 2,457 Life Span Study sample autopsies, the age-adjusted prevalence rate of primary carcinoma of the liver was 0.9% in Hiroshima and 2.6% in Nagasaki. In Hiroshima, 52.9% of carcinomas, 60% of hepatomas and none of the cholangiocarcinomas were associated with cirrhosis of the liver; 8.5% of the 106 pts. with cirrhosis had coexisting carcinoma. In Nagasaki, 64.7% of hepatic carcinomas, 76.9% of hepatomas and 25% of the cholangiocarcinomas were associated with cirrhosis; 29.7% of the 37 pts. with cirrhosis also had carcinoma. Post-hepatic cirrhosis was the type of cirrhosis most commonly found in association with a hepatoma. No relationship was seen between ionizing radiation and primary carcinoma of the liver. The higher rate of carcinoma in Nagasaki can be partly explained by the greater tendency in that city for cirrhosis to be associated with a hepatoma.

- 70-2560 A HISTOPATHOLOGIC STUDY ON THE EFFECT OF ALCOHOL ON CIRRHOSIS AND HEPATOMA OF AUTOPSY CASES IN JAPAN. (E.) Sakurai, M. (Osaka U. Med. Sch., Japan). *Acta Path. Jap.* 19(3):283-314, 1969.

A survey of 2928 autopsied pts. for whom clinical histories were available and 238 medical examiner's autopsy cases, disclosed 199 cases of cirrhosis and/or hepatoma. In the larger series, the male:female ratio was 2:1; cirrhosis and hepatoma were found in 111/1904 males (5.8%) and 22/1024 females (2.1%), including 52 cases of cirrhosis with hepatoma, and 10 of hepatoma without cirrhosis. Alcoholism, primarily from drinking rice wine (sake), was 13 times more prevalent in males than in females. Males comprised 83% of the pts. with cirrhosis. Only 49% of the alcoholic pts. had cirrhosis. As alcohol intake increased, the association with hepatoma decreased. Only 20/52 pts. (38%) with cirrhosis and hepatoma were alcoholics. Toxic

anges induced by rice wine were relatively d; "alcoholic hyaline" was rare, and only 1 e of florid cirrhosis was noted. Rice wine- uced cirrhosis progressed from the early ritional type to the posthepatic type; 43/52 . (83%) with cirrhosis and hepatoma showed hepatic type cirrhosis, although 27/43 %) were not alcoholics. The preparation of a wine includes treatment with fungi; the sible role of a mycotoxin in the induction hepatoma is briefly discussed.

2561 THE EPIDEMIOLOGY OF PRIMARY CARCINOMA OF THE LIVER. (E.) Higginson, J. . Agency Res. Cancer, London). Recent ults Cancer Res. 26:38-52, 1970.

mination of the rates of hepatic carcinoma ined from cancer registries in 23 countries ed primary liver cancer to be uncommon in h and South America, Western Europe, the S and Australia. Countries with high tumor idence had increased incidence predominantly he younger age groups. Countries of low r tumor incidence compared to those of high idence had about 10-20% and 60-70% cirrhotic rs showing malignant change, resp. This tion between cirrhosis and liver cell cancer ot causal; both may represent different restations of the same stimulus. The roles rrhosis, malnutrition, ethanol ingestion, ological agents (viruses, parasites), chemical rogens and naturally occurring carcinogens u as *Senecio* alkaloids, cycasin and aflatoxin) e etiology of primary liver carcinoma are ssed. The epidemiological distribution of y, cancer suggests that environmental factors, nborn genetic or racial factors, are of significance. A 2-stage hypothesis for opment of primary liver cancer is outlined.

2562 EPIDEMIOLOGY OF BREAST CANCER. (E.) Davies, J. N. P. (Albany Med. Coll.,). Int. J. Cancer 5(1):157, 1970.

Comparison of the histological grades of breast cs found in 174 women and 21 men from Uganda w a striking difference in malignancy; c III tumors (the Bloom-Richardson grading) e found in 50% of the women and 10% of the . By comparison, 80% of 100 tumors among ean women, and 29% of 1544 tumors among h women, were of Grade III malignancy. ults suggested that breast cancer in n women is much lower in incidence than in h women, but more malignant when it does ep. It is suggested that the high malignancy ast cancer in African women may represent ase phenomenon from a strong repressor or agencies.

2563 ESTIMATING THE NUMBER OF UNNECESSARY DEATHS FROM BREAST CANCER. (E.)

Podell, R. N. (107 Louis Pasteur Ave., Boston, Mass.). J. Chron. Dis. 2(6/7):451-462, 1969.

Several mathematical models of breast cancer mortality, based upon data from previously published reports (notably from the University of Minnesota, the California Tumor Registry and 2 American insurance companies) are presented, emphasizing the relationships among early or late detection, delay, survival and curability. It is suggested that, in addition to survival time, mortality rate from breast cancer be used to estimate benefits from early detection and treatment.

70-2564 BREAST CANCER FOUND ON REPETITIVE EXAMINATION IN MASS SCREENING. (E.) Strax, P. (1056 Fifth Ave., New York, N. Y.), L. Venet, S. Shapiro, S. Gross and W. Venet. Arch. Environ. Health (Chicago) 20(6):758-763, 1970.

Control (women who received medical care as in the past) and experimental groups of women aged 40-64-yr., each totaling 30,000, were randomly chosen for clinical examination and mammography for detection of breast cancer. A total of 65% of the experimental group appeared at initial screening and most of these appeared for the 3 additional screenings at annual intervals. Detection rate at initial examination was 2.72/1000 (55 tumors) compared to 1.44/1000 in the control women. Of these 55 tumors, clinical examination or mammography detected 44% and 38%, resp.; 18% of the tumors were detected by both modalities. Subsequent screenings revealed 63 more cancers (46%, 30% and 24% on clinical examination, mammography or a combination). If mammography or clinical examination had been omitted, 34% and 45% of the total cancers, resp., would have gone undetected. Absence of axillary nodal involvement remained substantially higher in the screened than the control group. At subsequent screening, over-all figures for lack of lymph node involvement were 75% compared to 44% for controls. Information is presented on the relation between size and type of breast and modality of detection.

70-2565 LACTATION AND CANCER OF THE BREAST. A SUMMARY OF AN INTERNATIONAL STUDY. MacMahon, B. (Harvard Sch. Public Health, Boston, Mass.), T. M. Lin, C. R. Lowe, A. P. Mirra, B. Ravnihar, E. J. Salber, D. Trichopoulos, V. G. Valaoras and S. Yuasa. Bull. WHO 42(2): 185-194, 1970.

The relation between the duration of lactation and the risk of breast cancer was studied in an international survey. The pts. and their resp. controls were from 2 areas of high-breast cancer incidence (Boston, Massachusetts; Glamorgan County, Wales), 3 areas of intermediate incidence (São Paulo; Athens; Slovenia, Yugoslavia) and 2 areas of low incidence (Taipei, Taiwan; Tokyo

Prefecture). The international difference in breast cancer incidence was particularly marked in the older age groups. Although pregnancy conferred some protection against breast cancer in all areas studied, no consistent differences between the pt. groups and the controls were found with respect to duration of lactation (with data adjusted to compensate for the smaller number of pregnancies among the cancer pts. as compared to the controls). Even in regions where some women had nursed their children for a total of 5 yr. or more, such prolonged lactation was about equally frequent in the cancer pts. and the controls.

70-2566 LACTATION AND REPRODUCTIVE HISTORIES OF BREAST CANCER PATIENTS IN TOKYO, JAPAN. (E.) Yuasa, S. (Inst. Public Health, Tokyo) and B. MacMahon. Bull. WHO 42(2):195-204, 1970.

Data on the influence of the reproductive history on the risk of breast cancer were obtained by interview of 849 women with breast cancer and a group of control women, admitted to Tokyo hospitals over a 2-yr. period. Elevated breast cancer risks were associated with the unmarried state, prolonged residence in Tokyo Prefecture (10 yr. or more), high socio-economic status (determined by educational level), Histories of 1 or more abortions, nulliparity (among the married women only), early menarche, late pregnancy and (of borderline significance) menopause after the age of 50 yr. Late age at menarche (17 yr. or over) and early age at first pregnancy were associated with a reduction in the breast cancer risk. The breast cancer risk in women who first became pregnant at or over age 35 yr. was 3.6 times higher than the risk in women who became pregnant under the age of 20 yr. Lactation was not associated with a reduced breast cancer risk; even very prolonged lactation (120 mo. or more) had no significant protective effect.

70-2567 CANCER OF THE FEMALE BREAST. 2. MARRIAGE AND FERTILITY IN CANCER OF THE BREAST. (E.) Lin, T.-M. (Nat. Taiwan U. Coll. Med., Taipei), R.-T. Ko and K.-P. Chen. J. Formosan Med. Ass. 69(3):164-173, 1970.

During the 10yr. period 1954-1963, 1098 women died from breast cancer in Taiwan. The breast cancer death rates/100,000 population during this period were higher in single women than in ever-married women at all ages over 30 yr., but the data were not considered conclusive. Examination of the 1952-1963 mortality and fertility statistics (crude birth rate, general fertility rate, and total fertility rate) for areas within Taiwan (5 cities and 17 counties) showed strong inverse correlations between breast cancer death rate and all 3 measures of fertility. For total fertility, the inverse correlation

increased with increasing age. Study of published international statistics (23 nations) correlating total fertility rates in 1950-1955 with breast cancer death rates in 1962-1963 did not yield similar correlations. However, with analyses progressively restricted to countries with a smaller change in birth rate between 1920 and 1960, the inverse correlation increased.

70-2568 RELATION OF GRAVIDITY AND AGE TO PROGNOSIS AND CLINICAL STAGE IN UTERINE CERVIX CANCER. (E.) Kurohara, S. S. (U. Southern California Med. Ctr., Los Angeles), M. A. Selim and J. B. Graham. Cancer 26(1):39-45, 1970.

The relation of gravidity and age to prognosis and clinical stage was evaluated in 4,546 pts. with primary uterine cervix cancer observed from 1920-53 at the Roswell Park Memorial Institute. The 5-yr. survival rates were about 5-10% higher in pts. who had had 1-3 pregnancies before developing cervix cancer than in nulliparous women or grand multiparas (6 or more pregnancies). Lower survival rates associated with more advanced disease were seen in nulliparous women and pts. with many prior pregnancies. With increasing age and with increasing time after their last pregnancy, this relationship of gravidity to prognosis and clinical stage disappeared. It is possible that variations may be explained by certain physiopathological changes occurring in the cervix with successive pregnancies and age.

70-2569 STATISTICAL METHODS IN A SCREENING PROGRAM FOR CANCER. (E.) Renwick, D. H. G. (828 W. 10th Ave., Vancouver, British Columbia). Canad. J. Public Health 60(7):267-278, 1969.

Use of mechanical data processing methods in a program of screening for pre-clinical cervical cancer in British Columbia is described. At time of report, there was a close relationship between the development of the program and declining incidence. The incidence rate in the unscreened population was about 6-fold higher than among screened women. The incidence of clinical squamous carcinoma of the cervix in the female population of British Columbia 20 yr. of age or over, decreased from 27.8/100,000 in 1955-56 to 14.1/100,000 in 1965-66. From 1961-1966, the incidence rate among screened adult females was 4.5/100,000, while among unscreened females it was 27.3/100,000.

70-2570 AN ANALYSIS OF THE PREVALENCE AND INCIDENCE OF GYNECOLOGIC CANCER CYTOLOGICALLY DETECTED IN A POPULATION OF 175,767 WOMEN. (E.) Kasper, T. A. (U. Alberta, Edmonton, Canada), F. S. O. Smith, P. Cooper, J. Clayton and D. Todd. Acta Cytol. (Balt.) 14(5):261-269, 1970.

1960-1968 (inclusive), 283,543 cervical pathological specimens were obtained from 175,767 women residing in all parts of Alberta. About 1000 women were examined at least twice, for a total of 146,000 pt.-yr. of observation. Of the 1 genital tumors found, 1090 were detected histologically. Of the carcinomas in situ, 2840 were detected only at the second or subsequent examination; 85 of these were accepted as "true cytological converters" to malignancy. Data suggested that the generation of new carcinomas in situ begins at a very significant age in the 20-24-yr. age group, and that newly appearing carcinomas in situ develop 6-fold more frequently in women under 45 than in older women. It was also concluded that the earliest identifiable stage of carcinoma in situ develops about 8-10 years before the disease reaches its midstage of development.

2571 CERVIX CANCER CONTROL IN LOUISVILLE, KENTUCKY. (E.) Christopherson, W. M. (Louisville Sch. Med., Ky.). W. M. Mendez, A. Ahuja, F. E. Lundin, Jr. and J. E. Parker. *Am. J. Obstet. Gynec.* 26(1):29-38, 1970.

Effects of a 12-yr. (1956-68) mass cytological screening program in Louisville and Jefferson County, Kentucky, upon incidence rates of cervical uterine cancer are reported. Expected rates calculated from a preceding 3-yr. period in which screening was not performed. During the 12-yr. period, the av. annual rate of all cervical uterine cancers (including carcinoma in situ) was 25.5/100,000 women (20 yr. old or over). Throughout the study period, nonwhite women (all of whom were Negroes) comprised an av. 19% of the population of women aged 20 and over. The cervical cancer detection rates were higher in the nonwhite women than in the white women. Socio-economic status, however, measured more closely than race. During the last 12 yr. (1965-1967), a marked increase was seen in the proportion of cases of invasive squamous cell carcinoma of the cervix diagnosed in stage I, with the age-adjusted rates (proved cases) decreased 38%. The decrease was more pronounced in Caucasian women than in Negro women, and more marked in women less than 50 yr. old for both periods than for those 50 yr. old or over. The incidence of carcinoma in situ increased progressively from 9.4/100,000 women in 1953-1955 to 22.1/100,000 in 1965-67. The incidence of intrauterine carcinoma (age-adjusted to the incidence of the U.S. in 1950) increased from 2.0/100,000 women for the first period to 3.4/100,000 in the last period. Women less than 40 yr. old showed the greatest response to screening; older women were less inclined to undergo cytological screening.

2572 RACIAL FACTORS IN INVASIVE CARCINOMA OF THE UTERINE CERVIX. (E.) Jameson, J. (Nat. Women's Hosp., Auckland, New Zealand).

Aust. New Zeal. J. Obstet. Gynaec. 9(4):258-261, 1969.

From June, 1946 to December, 1965, a total of 1116 cases of invasive carcinoma of the cervix were diagnosed in New Zealand. These included 147 who were Polynesian by birth (Maori or Pacific Islander), 967 Caucasians and 2 Asians (1 Chinese, 1 Indian). In 1947 the age-adjusted mortality rate in New Zealand from cancer of the genital tract among Maoris was 34.5/100,000/yr., compared with 22.9 for Europeans. In the Auckland area, where 8.1% of total gynecological admissions to hospital were Polynesian, the expected incidence of invasive carcinoma was 8.1% of 1116, or 90 cases, but the actual incidence was 147 (13.7%), a highly significant excess. Only 66% of Polynesians presented to a physician when the carcinoma was at a "curable" stage (I or II), compared to 79.5% non-Polynesians. While 50% of non-Polynesians reported within the first 3 mo. of appearance of symptoms, only 40% of Polynesians did so. Age at onset was 1 decade earlier among Polynesians. The 5-yr. survival rate of Polynesians was poorer than in non-Polynesians, but similar when analysis was limited to Stage I cases.

2573 CARCINOMA CERVIX UTERI. (A CLINICO-PATHOLOGICAL STUDY OF 640 CASES.). (E.) Hafeez, M. A. (Gandhi Med. Coll., Bhopal, India) and P. L. Tandon. *Indian J. Cancer* 6(3):184-189, 1969.

During the yr. 1957-1968, inclusive, 1359 cases of cancer were reported for females in Bhopal, India; 706/1359 (51.9%) were cancer of the genital tract and 640/706 (90.5%) had carcinoma of the cervix. Age range was 20-75 yr., with 212/706 (33.1%) cases being from 41-50 yr. old and 201/706 (31.1%) being from 31-40-yr.-old. Moslem women, who constituted 13.8% of the female population studied, comprised 8.1% of the cases of cervical carcinoma, indicating a higher incidence of carcinoma among Hindu women. This reduced incidence in Moslems is most probably due to the practice of circumcision in Moslem males.

2574 INCIDENCE OF SURGICAL STERILIZATION IN PATIENTS WITH CARCINOMA OF THE CERVIX UTERI. (E.) Bosch, A. (I. Gonzalez Martinez Hosp. Puerto Rico Nuclear Ctr., San Juan) and Z. Frias. *Amer. J. Obstet. Gynec.* 104(8):1131-1137, 1969.

The frequency of sterilization by tubal ligation was studied in a group of 463 consecutive cases of uterine cervix carcinoma in pts. less than 50 yr. old, seen in Puerto Rico from January 1, 1959 to December 31, 1966. Factors analyzed in sterilized (173) and non-sterilized (290) pts. and in a population sample of women under 50 included age, parity, number of marriages,

socio-economic level, age at first marital relations, age at sterilization and interval between operation and cancer diagnosis. No significant difference was found between the age-adjusted sterilization rate of the cancer group and of the normal population sample. Sterilized cancer pts. were younger than those in the average cancer series, but were similar to nonsterilized pts. in other respects. In general, cancer was diagnosed an av. of 12 yr. after sterilization.

- 70-2575 COMPARATIVE RESULTS OF PROPHYLACTIC ONCOLOGICAL EXAMINATIONS IN WOMEN. (Rus.) Manelis, M. E. (Krivoi Rog City Oncol. Dispen., USSR). Akush. Ginek (Moskva) 45(3): 26-29, 1969.

Results of screening studies performed in 1966-1967 are discussed. In women undergoing 1-stage or 2-stage examinations without colposcervicography, carcinoma of the cervix was detected in 2/5088 (0.39%) and 3/46,118 (0.006%), resp., and premalignant lesions of the cervix in 55/5088 (1.08%) and 782/46,118 (0.006%), resp. When colposcervicography was added to the 1-stage and 2-stage examinations, cancer of the cervix was detected in 6/500 (1.2%) and 7/5769 (0.12%), resp., and premalignant lesions of the cervix in 160/500 (32%) and 212/5769 (3.7%), resp. Stage 0 and I carcinomas of the cervix, premalignant lesions of the cervical canal and the vaginal end of the cervix, and benign lesions of the mucosa of the cervical canal, were readily detected by colposcervicography, whereas screening methods not using colposcervicography detected only Stage II or III carcinomas and premalignant lesions of the cervix (including the vaginal portion of the cervical canal in a small number of cases).

- 70-2576 ANTIBODIES TO Herpesvirus hominis TYPES 1 AND 2 IN HUMANS. II. WOMEN WITH CERVICAL CANCER. (E.) Nahmias, A. J. (Emory U. Sch. Med., Atlanta, Ga.), W. E. Josey, Z. M. Naib, C. F. Luce and B. A. Guest. Amer. J. Epidemiol. 91(6):547-552, 1970.

Sera from 167 women with invasive and preinvasive lesions of the cervix, and an equal number of controls matched for age, race and socioeconomic status, were studied for Herpesvirus hominis (HVH) Type 1 and 2 antibodies by the micro-neutralization test. Type 2 and dual antibodies to HVH were found in sera from 83% of the pts. with invasive carcinoma, 70% of pts. with carcinoma in situ, 56% of the pts. with cervical dysplasia (identified histologically) and 40% of pts. with cervical atypia (diagnosed by cytological examination only). In the corresponding control groups, the frequencies of NVH antibodies were 35%, 24%, 18% and 20%, resp. These findings indicate a definite association between genital herpes and anaplastic diseases of the cervix. Further studies are needed to determine if this association is causal.

- 70-2577 BACKGROUND OF STATISTICAL DATA ON OVARIAN CANCER. Randall, C. L. Pp. 211-219 in Gynecological Oncology. A Comprehensive Review and Evaluation, Barber, H. R. K. and E. A. Graber (Eds.). Williams & Wilkins Co., Baltimore, 1969, 386 pp.

Statistical data on the primary site of certain reported female genital tumors (breast, cervix, ovary) and age-adjusted rate/100,000 females in the state of New York (excluding New York City) for 1941-1966, revealed an ovarian cancer incidence rate of 10.7/100,000 females/yr. in 1941-43 and 11.6/100,000 in 1966, an increase of 7.6%. During the same time period, the death rate from malignant tumors of the ovary increased 16%, from 7.8 to 9.3/100,000 females. It is stressed that in comparison with other female genital cancer, the mortality from ovarian cancer is disproportionately great in relation to its incidence.

- 70-2578 MALIGNANT TESTICULAR TUMOURS IN FINLAND. (E.) Teppo, L. (U. Helsinki). Acta Path. Microbiol. Scand. 75(1):18-26, 1969.

During the period 1953-1961, 193 new cases of testicular tumors reported to the Finnish Cancer registry; paraffin-embedded samples of 131 tumors were obtained for re-evaluation. An av. of 21 testicular tumors/yr. (range, 12-28) was reported; the mean incidence rate/100,000 men/yr. was 1.0 new cases, which was less than rates reported from other nations (2.5 in Norway, 3 in Sweden, 2-3 in the U. S. and Britain). Of the 131 tumors re-evaluated, 48% were seminomas; embryonal carcinomas, teratomas and teratocarcinomas together constituted 40%, while malignant non-germinal tumors (including sarcomatous tumors) comprised 8%. These data on relative frequencies of tumor types were comparable to data from other Scandinavian nations, which showed a lower frequency of teratomatous tumors (34-40%) and a higher frequency of seminomas (50-58%) than in the U.S. (64% and 34%, resp.). In the total pt. group and the pts. with tumors of different types, age distributions and 3-5-yr. survival rates were comparable to those reported in the U.S. and Britain.

- 70-2579 EPIDEMIOLOGY OF PRIMARY CENTRAL NERVOUS SYSTEM NEOPLASMS. I. MORTALITY FROM PRIMARY CENTRAL NERVOUS SYSTEM NEOPLASMS IN MINNESOTA. (E.) Choi, N. W. (U. Manitoba, Winnipeg, Canada), L. M. Schuman and W. H. Gullen. Amer. J. Epidemiol. 91(3):238-259, 1970.

During 1958-1962, 760 pts. died with primary brain tumors in Minnesota. A bimodal curve of age- and sex-specific mortality rates, and a significant sex difference in the proportional distribution of tumor types, were noted. No geographical gradient of the rates (by county)

different rates by occupation were noted. Residents, who comprise 18.5% of the total population and 15.9% of the total female population of Minnesota, accounted for 26.9% of the males and 15.6% of the females with brain tumors. An excess of neurofibromatosis and acoustic tumors occurred in both males and females of this group; gliomas and blood vessel tumors occurred in excess in males only. A possible association between brain tumors and toxoplasmosis is suggested. Annual death rates/100,000 population in the native-born were 4.71 in males and 3.63 in females, compared to 13.35 and 8.64, resp., in foreign-born. The differentials between native-born and foreign-born rates were more marked in younger than older persons.

2580 EPIDEMIOLOGY OF PRIMARY CENTRAL NERVOUS SYSTEM NEOPLASMS. II: CASE-CONTROL STUDY. (E.) Choi, N. W. (U. Manitoba Fac. Med., Winnipeg, Canada), L. M. Schuman and W. H. Gullen. *Can. J. Epidemiol.* 91(5):467-485, 1970.

A group of 157 adults and children with brain tumors (from 4 hospitals in the Minneapolis-St. Paul metropolitan area) and 157 matched controls were studied. A familial aggregation of brain tumors was noted among relatives of the pts. No specific association was seen between tumors of different types and the ABO or Rh blood groups. Series of abnormal delivery (including forceps delivery and cesarean section) were much more frequent among the pts. with brain tumors than among the controls, especially in children with gliomas. A significant association was also noted between the occurrence of gliomas and histories of abortions prior to the probands' birth among mothers of the pts. Primary brain tumors were not associated with past histories of brain injury and previous illnesses, with the exception of certain symptoms prior to diagnosis, which might have been related to the tumors. Cigarette smoking and alcohol consumption were negatively associated with the tumors. No association between brain tumors and pipe or cigar smoking was found.

2581 DEMOGRAPHY OF TUMORS OF THE CENTRAL NERVOUS SYSTEM AMONG THE BANTU (AFRICAN) POPULATION OF THE TRANSVAAL, SOUTH AFRICA. (E.) van der Merwe, C. (Baragwanath Hosp., Johannesburg, South Africa) and R. Lipschitz. *J. Neurosurg.* 32:660-664, 1970.

Records of the Baragwanath Hospital for 1953-1968 (inclusive) disclosed only 213 primary brain tumors among the estimated 1,000,000 persons served by this hospital. Brain tumors comprised 0.006% of all hospital admissions in 1953 (before the establishment of a neurological department) and 0.026% of all admissions in 1964-1968 (the period of a 5-yr. prospective survey). This absolute incidence was 10-100 times lower than in general hospitals serving

Caucasian populations. The meningioma:glioma (adulthood) ratio in this series of tumors was 2:1 (the reverse of the pattern of incidence reported for Caucasian populations). Only 1 acoustic neurinoma was found during the entire 20-yr. period (in a comparable study in Sweden, the expected number of acoustic neurinomas in a similar population over a 20-yr. period was 100). The geographical distribution of the pts. corresponded roughly to the population densities in the region.

70-2582 ANALYSIS OF FLUCTUATIONS IN THE FREQUENCY OF TUMORS OF THE POSTERIOR CRANIAL FOSSA. (Pol.) Szydlowska, H. (Neurosurg. Clin., Cracow, Poland) and E. Szwagrzyk. *Folia Med. Cracov.* 12(2):285-294, 1970.

Analysis of records from the Neurosurgical Clinic of the Cracow Medical Academy from 1946-1967 inclusive revealed that the proportion of tumors of the posterior cranial fossa (annual percentage of operated intracranial tumors) showed no periodic variations, but did exhibit a rising trend. The proportion of astrocytomas and medulloblastomas of the posterior fossa (annual percentage of operated posterior fossa tumors) showed similar rising trends but no periodic fluctuations. These findings indicate that these 2 types of tumors originate from neuroectodermal, rather than from mesenchymal tissue. A rising trend was also noted in the frequency of supratentorial glial tumors (annual percentage of operated supratentorial tumors). The proportion of connective tissue tumors of the posterior fossa (annual percentage of operated posterior fossa tumors) and supratentorial connective tissue tumors (annual percentage of operated supratentorial tumors) showed periodic fluctuations, reaching a max. every 5 yr. There was a 2-3-yr. difference in the max. frequencies of these 2 groups of connective tissue tumors. This difference could be explained by differences in the ratio of meningiomas to sarcomas. No evidence of an increase or decrease could be found for the frequency of neurinomas over this 22-yr. period.

70-2583 MALIGNANT TUMORS OF HEAD AND NECK IN CHILDHOOD. (E.) Berge, T. (Gen. Hosp., Malmo, Sweden) and N. G. Toremal. *Acta Otolaryng.* (Stockholm) 68(6):551-560, 1969.

During the 10-yr. period 1958-1967 in the defined population of Malmo, Sweden, malignant tumors were diagnosed in 31/612 (5.1%) autopsied children below 15 yr. of age (total deaths, 739; autopsy rate, 83%). Leukemia caused death in 13/31 (42%) cases. The group included 8 pts. with malignant tumors originating in the head and neck region, including 1 with embryonal rhabdomyosarcoma of the mandible and floor of the mouth, 1 with Ewing's sarcoma of the skull and 1 with reticulum cell sarcoma of the neck

(not autopsied). Incidence of malignant tumors of the head and neck in childhood was 0.3/100,000/yr., which was 10-fold higher than that reported in East Germany over a 5-yr.-period (0.03/100,000/yr.).

70-2584 INCIDENCE AND PROGNOSIS OF SALIVARY-GLAND TUMOURS AT DIFFERENT SITES. A STUDY OF PAROTID, SUBMANDIBULAR AND PALATAL TUMOURS IN 2632 PATIENTS. (E.) Eneroth, C.-M. (Karolinska Hosp. Inst. Tumor Path., Stockholm). *Acta Otolaryng.* Suppl. 263:174-178, 1970.

In 1909-1965 (mainly 1925-1965), 2632 pts. were treated at Karolinska Hospital for palpable lesions of the parotid, submandibular and palatal regions. True salivary gland tumors were found in 2311 pts. (87.8%). Benign lesions, mostly pleomorphic adenomas, accounted for 1638/1983 parotid tumors, 100/161 submandibular gland tumors and 93/167 tumors of the palatal salivary gland. Most of the malignant tumors (17% of the parotid tumors, 38% of the submandibular gland tumors and 44% of the palatal salivary gland tumors) were malignant mucoepidermoid carcinomas, while 2%, 16% and 22%, resp., were adenoid cystic carcinomas. For a given type of tumor, the site influenced the prognosis. Prognosis appeared to be most favorable with tumors of the palatal salivary gland, intermediate with tumors of the parotid gland and least favorable with tumors of the submandibular gland.

70-2585 CLINICAL AND PATHOLOGIC ANATOMICAL STUDY OF 31 MEDULLARY CARCINOMAS OF THE THYROID WITH AMYLOID STROMA. (Fr.) Muller, M. (27 Ave. Tribunal Federal, Lausanne, Switzerland). *Schweiz. Med. Wschr.* 99(13):433-439, 1969.

Medullary carcinoma of the thyroid with amyloid deposits in the stroma was found in 31 pts. (15 men, 16 women; mean age 43.2 yr.). None showed distant metastases at the time of surgery, but 13/31 showed cervical lymph node metastases, 3/31 showed metastatic tumors limited to the thyroid, and in 5/31, the thyroid capsule was invaded. In 2/31, the disorder was associated with a subsequent pheochromocytoma; in 11/31, with intercurrent diarrhea, which ceased upon removal of the tumor. Diarrhea recurred in 3/11 when subsequent hepatic metastases (2/3) or pheochromocytoma (1/3) developed. However, it failed to recur in 2/11 who later developed pulmonary metastases. There was no discernible relationship between subsequent development of distant metastasis and sex, degree of amyloid deposition, histologic characteristics of the tumor, or association of diarrhea with the primary disorder. The pts. constituted 5.1% of a total of 600 malignant tumors of the thyroid, found among about 16,000 extirpated goiters.

70-2586 LYMPHOID TISSUES IN NEOPLASIA. A PILOT STUDY AND REVIEW. (E.)

Kessler, I. I. (Johns Hopkins U. Sch. Hyg. Public Health, Baltimore, Md.). *Cancer* 25(3): 510-522, 1970.

A study of 919 consecutive autopsies at the Kings County Hospital Center in 1960, and of interviews and physical examination in 461 cancer pts. and 223 controls from 2 New York hospitals in 1965, failed to show any relationship between prior appendectomy and tonsillectomy and subsequent risk of cancer. In the autopsy series, no analysis of tonsillectomy frequency was attempted, but the number of expected and observed appendectomies was 11 and 7, resp., among men with cancer and 11 and 10, resp., among women. Differences were not considered significant. In the interview series, the appropriately weighted relative risks of appendectomy and tonsillectomy were 0.72 and 1.26, resp., in men with cancer and 1.12 and 1.06, resp., among women. Differences were again not significant. In general, there were too few pts. in the various age categories to allow an age-adjusted statistical analysis of lymphoid tissue surgery among pts. with specific types of cancer and their controls. However, the relatively small sample sizes of pts. with particular neoplasms do not permit the rejection of the possibility that a 2- or 3-fold deviation in relative risk actually exists for pts. with certain types of cancer.

70-2587 IS APPENDECTOMY FOLLOWED BY INCREASED CANCER RISK? (E.) Berndt, H. (Inst. Cancer Res. Robert Rossle Clin., Berlin-Buch). *Digestion* 3(3):187-191, 1970.

A survey of the frequencies of appendectomy (appx.) in all hospitals of Berlin during 1963 led to the estimate of a lifetime appx. frequency of about 3.5% in males and 4.3% in females in Berlin (compared to about 4.9% and 6.2%, resp., in Frankfurt). The higher appx. rate in females was attributed to the difficulties of differential diagnosis between appendicitis and gynecological diseases in younger women. Histories of appx. were noted for 129/2234 males with lung cancer (5.8%), 15/215 with stomach cancer (7.0%) and 34/548 with cancer of the colon and rectum (6.2%) at the author's hospital. Even higher rates were found among other in-patients without cancer, 54/423 (12.8%) of male pts. without cancer and 32/203 (15.8%) of male pts. with peptic ulcer. In view of various methodologic considerations (choice of controls, temporal trends, socio-economic differences), it is concluded that pts. with histories of appx. are over-represented in a hospital population, and that a relationship between appx. and these cancers can be considered unlikely.

70-2588 SEROLOGIC SURVEYS OF HUMAN CANCER PATIENTS FOR ANTIBODY TO ADENOVIRUS T ANTIGENS. (E.) Gilden, R. V. (Flow Labs. Inc., Rockville, Md.), J. Kern, Y. K. Lee, F. Rapp,

L. Melnick, J. L. Riggs, E. H. Lennette, B. r, H. J. Rapp, H. C. Turner and R. J. Huebner. J. Epidemiol. 91(5):500-509, 1970.

from 197 pts. with advanced solid tumors and 192 control subjects were tested for antibodies to the T antigens of oncogenic adenoviruses of human (subgroups A, B and C) or other origin (bovine type 3, canine hepatitis, simian adenovirus subgroups I, II and III). No indication of antibody activity was found in any of the sera to any of the viral T antigens by complement fixation tests. Sera reacting with the preparations of human adenovirus subgroups B and C were eliminated by the use of partially purified antigens and antigen-containing transfected rat embryo cells. One serum reacted to an adenovirus group C, as well as SV20-transfected rat cells, SA-7 and normal rat cells; a serum and several others reacted with nearly any preparation studied, including normal sera. A small percentage of sera reacted in the rescent antibody test with uninfected African monkey kidney cells; an additional small percentage of sera reacted with some antigens produced by adenovirus Types 2, 7 and 12, but the occurrence of such reacting sera was about the same in the controls as in sera from the cancer patients. It is concluded that antibodies against adenovirus T antigens are about equally prevalent in sera from cancer pts. and controls.

2589 INCIDENCE OF ANTIBODIES TO ADENOVIRUS-ASSOCIATED VIRUSES IN PATIENTS WITH TUMORS AND OTHER DISEASES. (E.) Sprecher-Berger, S. (Brabant Pasteur Inst., Brussels), Hekegel, J. Otten and L. Thiry. Arch. Ges. Viroforsch. 30(1):16-21, 1970.

from 12 children and 21 adults with unfixed tumors were compared to sera from 20 children and 44 adults with other diseases, for the occurrence of antibodies to adenovirus-associated virus (AAV) Type 3; most sera were assayed with Type 1 and 2 antigens. Antibodies to AAV Type 3 were found in 9% of the sera from cancer pts. (8% in children, 9.5% in adults), compared to 31% of the control sera (5% in children, 29.5% in adults). A similar, nonsignificant difference was noted in the presence of antibodies to AAV Type 1 (19% of sera from cancer pts., 29% of control sera). Type 2 antibodies were equally frequent in both groups. The results were consistent with the hypothesis that adenovirus infections in man carry some risk of cancer, but that this risk is increased in the presence of AAV.

30 SEASON AND THE ONSET OF ACUTE CHILDHOOD LEUKEMIA. (E.) Fekety, F. R., J. Michigan Med. Sch., Ann Arbor) and H. Carey. Maryland Med. J. 18(11):73-77 & 369.

Seasonal variations in onset were studied in 96/107 leukemia pts., who were under 20 yr. old at the time of admission to the Johns Hopkins Hospital, between 1950-1962. In about 49% of cases, the clinical onset (earliest date at which definite evidence of the disease was present) was from May to August; in 17%, the clinical onset was from September to November; diagnosis was made between June and September in 44.7%. This seasonal variation was especially evident in pts. with acute lymphocytic or stem cell leukemia, in girls, in Caucasians, in pts. whose parents were under 35 yr. old at the time of the pts.' birth, and in residents of the Greater Baltimore area or of Maryland outside of Baltimore. No significant seasonal variation was seen in the dates of birth, blood type or initial clinical features.

70-2591 AUSTRALIA ANTIGEN (A HEPATITIS-ASSOCIATED ANTIGEN) IN LEUKEMIA. (E.) Sutnick, A. I. (Inst. Cancer Res., Philadelphia, Pa.), W. T. London, B. S. Blumberg, R. A. Yankee, B. J. S. Gerstley and I. Millman. J. Nat. Cancer Inst. 44(6):1241-1249, 1970.

In a study of the relationship of the Australia antigen (Au(1)) to leukemia and Hodgkin's disease, blood tests of leukemia pts. and those with Hodgkin's disease showed 48/688 (7%) and 5/80 (6.3%), resp., had Au(1). Frequency in the normal U.S. population is 0.1%. Frequency was similar for lymphocytic, chronic lymphocytic and acute myeloid leukemia (9.8%, 6.7% and 9.0%, resp.), but was lower in chronic myeloid leukemia (2.7%). In 512 leukemia pts., an association of Au(1) with previous blood transfusion was also demonstrated. Chemotherapy and radiotherapy showed no such association. It is concluded that Au(1) does not cause leukemia, but rather that a high degree of susceptibility to chronic infection with Au(1) virus exists for leukemic pts. It is suggested that Au(1) occurs primarily as a result of blood transfusion, and persists thereafter. The data also support a hypothesis that some abnormal susceptibility to both Au(1) virus and leukemia exists in certain populations. Both conclusions could explain the high frequency of association of Au(1), leukemia and Down's syndrome.

70-2592 RELIGION AND ETHNICITY IN LEUKEMIA. (E.) Graham, S. (State U. New York Sch. Med., Buffalo), R. Gibson, A. Lilienfeld, L. Schuman and M. Levin. Amer. J. Public Health 60(2):266-274, 1970.

In 1959-1962, 319 cases of leukemia in children and 1414 cases in adults were reported in 3 metropolitan-area surveys (New York State excluding New York City, Minneapolis and Baltimore). The leukemia pts. were compared to appropriate control groups to study the effects of religious

and ethnic background and histories of irradiation on the relative risk of leukemia. No differences with respect to any demographic parameter were found among the children. Among American-born adults, the relative risk among Jews, as compared to non-Jews, was 2.44. In Russian-born adults and in Russian Jews, the relative risks as compared to American-born adults whose parents were born in Eastern Europe, were 2.91 and 4.3, resp.; as compared to American-born adults whose parents were not born in Eastern Europe, these relative risks were 3.81 and 5.29, resp. In Polish-born adults, the relative risks as compared to American-born adults of Polish-born or American-born parents, were 3.9 and 2.12, resp. The Polish-born group included very few Jews. No convincing evidence of a high leukemia risk was found among Jews of non-Eastern European background. Irradiation did not seem to account for an excess leukemia risk in either Jews or non-Jews. The excess leukemia risks among Jews (especially Russian Jews), Russians and Poles decreased when these groups were compared to other populations of culturally similar backgrounds.

70-2593 RACIAL VARIATIONS IN LEUKEMIA INCIDENCE AMONG THE ELDERLY. (E.) McPhedran, P. (Yale-New Haven Hosp., Conn.), C. W. Heath, Jr. and J. S. Garcia. *J. Nat. Cancer Inst.* 45(1):25-28, 1970.

Data collected from 1956-67 among residents of metropolitan Atlanta showed the over-all leukemia incidence in whites and Negroes (adjusted by 10-yr. groups to the age and sex distribution of the total population of the city in 1960) to be 8.4/100,000/yr. in whites and 5.1/100,000/yr. in Negroes. Rates for each race were similar in all age groups less than 70 yr. old, but after age 70 rates in whites rose steeply, whereas rates in Negroes showed no such rise. The low rate in elderly Negroes included all types of leukemia and each type was reduced to about the same degree (20% and 33% of the white incidence). In younger Negroes, acute leukemia was 69% of the white incidence and chronic lymphocytic leukemia was 67%, but no deficit was observed for chronic granulocytic leukemia. The deficit in elderly Negroes seems more to be due to unreliable population data or socioeconomic factors than with true racial variation.

70-2594 RELATIONSHIP BETWEEN THE NUMBER OF PREGNANCIES AND RISK OF ACUTE LEUKEMIA. (Fr.) Dausset, J. (St. Louis Hosp. Inst. Leukem. Res., Paris), L. Degos, B. Estampe and J. Bernard. *Nouv. Rev. Franc. Hemat.* 10(1):55-62, 1970.

In this study based on 164 women more than 18 yr. old with acute leukemia (120 acute myeloblastic, 44 acute lymphoblastic) and on data from the French population census of 1946, it was found that women with 0, 1 or 2 children develop acute

myeloblastic leukemia more frequently than those with 3 or more children. It is suggested that protection in the latter group derives from immunization against tissue surface antigens.

70-2595 HAPTOGLOBIN (Hp) AND Gc GROUP SYSTEMS IN LEUKEMIA PATIENTS. (Pol.) Gurda, M. (3rd Intern. Dis. Clin., Cracow, Poland). *Folia Med. Cracov.* 12(2):207-249, 1970.

Haptoglobin (Hp; qualitative and quantitative studies) and Gc groups were determined in 175 pts. with different types of leukemia (acute myeloblastic 52, chronic granulocytic 45, chronic lymphocytic 78) and different correlations (type of leukemia, sex and, in myeloblastic leukemia, age) were statistically analyzed and results compared to normal values as reported in the literature. In addition, Hp levels were determined before and after therapy in 26 pts. No correlation between type of leukemia, Gc and Hp distribution, Hp level, sex or age was detected. However, a relationship between Hp type and level was observed. The lowest levels were detected in Hp 2-1, highest in Hp 2-2. Mean levels of the homozygotic types (Hp 2-2 and Hp 1-1) were significantly higher than for the heterozygotic type (Hp 2-1). These results differed from those for healthy subjects where the Hp 1-1 level was highest and Hp 2-2 lowest. Therapy of myeloblastic leukemia (corticoids, blood transfusions) was followed by a significant increase in Hp level; treatment of chronic granulocytic leukemia with antimitotic agents gave a slight decrease and treatment of lymphocytic leukemia (as above) gave a distinct decrease in Hp levels. The distribution of Gc types among leukemia pts. was similar to that reported for a healthy population. No relationship to type of leukemia, sex or age was seen. Distribution of Hp types was similar to that of normal subjects, but the mean level reported (in mg% Hb) was significantly higher in all types of leukemia. The Hp level was similar to that reported for pts. with malignant tumors, inflammations and degenerative diseases. A few cases of ahaptoglobinemia were seen, but these were related to *in vivo* hemolysis; no type 0-0 Hp was detected among the leukemia pts. It is concluded that no relationship between susceptibility to or incidence of different types of leukemia and the Gc and Hp group systems exists.

70-2596 HIGH FREQUENCY OF LEUKEMIA. A COMPARISON OF LEUKEMIA INCIDENCE IN JAPAN AND THE WORLD. (Jap.) Hirayama, T. (Nat. Cancer Ctr., Tokyo). *Saishin Igaku* 24(11):2201-2204, 1969.

The leukemia death rate in Japan, in 1952-1963, was much lower than in other countries. In 1962-1964, the av. leukemia incidence rates in male and female Japanese were 105/100,000 and 72/100,000, resp. Deaths from acute leukemia

creased greatly from 1958 to 1966; from 798 to 57 deaths in males and from 183 to 246 in females. Myeloid leukemia was also prevalent in Japan, with 263 deaths in males and 185 in females in 1965. The leukemia mortality rates/100,000 population were 3.0 in large cities, 3.2 in smaller cities and 3.4 in rural areas.

-2597 AREAS WITH A HIGH FREQUENCY OF LEUKEMIA IN JAPAN. (Jap.) Kobayashi, H. Hokkaido U. Med. Sch., Sapporo, Japan), K. Kobayashi and H. Miyake. Saishin Igaku 24(11):2210-2213, 1969.

7 areas with the highest incidence of leukemia in Japan from 1958-1962 were Shizunai, Reizan, Hirakawa, Kabe, Yamato, Seihi and Kunimi. Of the total number of leukemia pts. from the above areas, 69.6% were male and 30.4% female. Half of the pts. were between 15 and 54 yr. old. Acute leukemia was seen in 63%. Farmers and fishers accounted for 28.3% of the pts. The peak frequency occurred in January and February, which is the resting period for farmers in Japan.

72598 HIGH FREQUENCY OF LEUKEMIA IN CHUGOKU AND NAGASAKI. (Jap.) Okita, T. (Hiroshima U. Inst. Atomic Med., Japan). Saishin Igaku 24(11):2222-2225, 1969.

From 1955-1968, 8 cases of acute and 3 cases of chronic leukemia were reported in 2 Japanese cities, Muika and Nishiki. No factors to account for this high frequency could be established. Studies showed an additional 7 pts. with Banti's syndrome in Muika City. Natural radiation of the 2 areas was 10-20 μ r/hour.

72599 HIGH FREQUENCY OF LEUKEMIA IN YUGAWARA, SHIZUOKA, JAPAN. (Jap.) Hirayama, T. (Nat. Cancer Ctr., Tokyo). Saishin Igaku 24(11):2225-2226, 1969.

Yugawara (Shizuoka Prefecture), Japan, 5 children (0-6 yr. old) were reported with acute leukemia in 1967-1969. The disease did not occur in any other age group. No special environmental or social factors in the town could account for the relatively high incidence of leukemia. Testing of 4/31 (12.9%) children of the town showed high antibody titers against Epstein-Barr virus, as seen in 3 of the leukemia pts.

72600 STUDY ON AREAS WITH A HIGH FREQUENCY OF LEUKEMIA. (Jap.) Mokuno, J. (Aichi Prefect. Cancer Ctr., Nagoya, Japan), H. Nishiyama and K. Ota. Saishin Igaku 24(11):2231-2238, 1969.

Testing for the period 1965-1966 showed 29 Japanese cities and towns with a frequency of more than 3 leukemia pts./yr. Kyoto had the

highest frequency, with 30 cases reported for the population of 131,207 in that yr.

70-2601 CAUSES OF A HIGH FREQUENCY OF LEUKEMIA. STATISTICAL RELATIONSHIP BETWEEN LEUKEMIA AND OTHER KINDS OF CANCER (ESPECIALLY BREAST CANCER, OVARIAN CANCER AND PROSTATE CANCER). (Jap.) Segi, M. (Tohoku U. Med. Sch., Sendai, Japan) and N. Kurihara. Saishin Igaku 24(11):2239-2244, 1969.

The annual mortality rate for leukemia in Japan in 1962-1963 was 6.32/100,000 population (lowest among 24 countries studied). The highest mortality rate (13.42/100,000) was observed in Israel. The low mortality rate in Japan was attributed to differences in age group distribution. Relative coefficients between mortality rates for leukemia and other kinds of cancer were determined. In the 0-15-yr. age group, leukemia was correlated with tumors of the esophagus in boys with tumors of the pharynx, ovary and skin in girls. No correlation between leukemia and other cancers was noted between ages 15-54 yr. In the over-55 yr. age group, leukemia was correlated with stomach cancer in both sexes, with cancer of the intestine, liver, biliary tract and prostate in men, and with cancer of the pharynx, breast and ovary in women.

70-2602 LEUKEMIA INCIDENCE FROM THE POINT OF VIEW OF RADIOLOGY. (Jap.) Okita, T. (Hiroshima U. Inst. Atomic Med., Japan). Saishin Igaku 24(11):2247-2251, 1969.

Studies of 158 pts. with leukemia who survived the atomic bombing in Hiroshima showed that the incidence of leukemia was lower in A-bomb survivors who had been beyond a 2-km range from the impact center. Chronic myeloid leukemia was observed in 49 pts. within the 2-km range and 8 pts. beyond 2 km. Acute leukemia was observed in 67 pts. within 2 km and 32 pts. beyond 2 km. The leukemia mortality rate/100,000 A-bomb survivors was 6.6 in 1950, 8.5 in 1955, 5.5 in 1960 and 7.9 in 1965, compared to 1.5, 2.3, 2.8 and 3.2 resp., for all of Japan for the same yr. The incidence of leukemia among A-bomb survivors in Hiroshima decreased between 1960 and 1965.

70-2603 LEUKEMIA IN SURVIVORS OF THE ATOMIC BOMBING. II. NAGASAKI. (Jap.) Ichimaru, M. (Nagasaki U. Sch. Med., Japan). Nippon Ketseuki Gakkai Zasshi (Acta Haemat. (Jap.)) 31(5):772-783, 1968.

From September, 1945 through the end of 1967, 583 proven cases of leukemia were found in Nagasaki. The incidence of probable radiation-induced leukemia has decreased recently, but 2-3 cases/yr. are still discovered. Younger persons seemed to be more sensitive to radiation-induced acute and chronic granulocytic leukemia than

persons in older age groups. Leukemia development in persons exposed to the A-bomb at early ages may have almost stopped. A linear relationship between radiation dosage and the leukemia incidence was noted at the higher radiation doses (49.64/100,000/yr. for all leukemias, 44.84 for acute leukemias, 6.40 for chronic leukemias, at radiation doses of over 120 r; compared to 5.30, 4.37 and 0.92, resp., at doses of less than 3 r). A linear dose-response relationship was not seen at radiation doses of 20-100 rads, suggesting the existence of a threshold. Several aleukemic leukemias (resembling aplastic anemia) were found in 1950-1955. Mild, atypical adult acute leukemias were characteristically found in proximal survivors in recent studies. Atomic radiation exposure apparently induced both acute granulocytic and acute lymphocytic leukemia, with a relatively high incidence of peroxidase-negative and undifferentiated leukemias in proximal survivors.

70-2604 SOME CONSIDERATIONS ON LEUKEMIA DEVELOPMENT AFTER THERAPEUTIC IRRADIATION. (Jap.) Kurokawa, S. (Niigata U. Sch. Med., Japan) and T. Kitabatake. Nippon Igaku Hoshasen Gakkai Zasshi (Nippon Acta Radiol.) 29(8):1081-1086, 1969.

In 1954-1966, 52 pts. with radiation-associated leukemia were reported in Japan. Of these, 30 originally had malignant or benign tumors, 5 tuberculosis, 5 dermatitis, 3 Basedow's disease, 5 hemangiomas, 1 gastric ulcer, 1 nasal polyp and 2 unknown diseases. In comparison with leukemias developing in the general population, the pts. with leukemia following irradiation were significantly older. The peak occurrence of radiation-associated leukemia was noted in the 50-54-yr. age group. Of the 52 pts., 31 developed acute myeloid leukemia, 10 chronic myeloid leukemia, 10 other forms of acute leukemia and 1 undifferentiated leukemia. The relationship between age and latent period and radiation doses and latent period was not established.

70-2605 GENETICS OF FAMILIAL LEUKEMIA. (Jap.) Kurita, S. (Aichi Cancer Ctr. Hosp., Nagoya, Japan) and Y. Kamei. Jap. J. Hum. Genet. 14(2):163-179, 1969.

Among 63 kindreds with familial leukemia observed in Japan, the relationships of other affected relatives to the proband were: sibling (1 or 2 siblings) in 27/63; parent or child in 12/63; grandparent or grandchild in 6/63; uncle, aunt, nephew or niece in 12/63; and first cousin in 6/63. No evidence for familial occurrence of the same type of leukemia was noted. Kinships between the proband's parents were known in 36 cases. Nine consanguineous marriages (5 of first cousins, 2 of first cousins once removed, 2 of second cousins) were found among the parents of

18 sibships with 2 or more cases of leukemia. Among the parents of 18 families in which a relative other than a sibling was affected, only 1 consanguineous marriage (second cousins) was noted. Among the parents of 200 pts. with non-familial leukemia, 9 first-cousin marriages were discovered. Consanguineous marriages were significantly more frequent in the leukemic sibships than in the other families. Siblings whose parents were related developed leukemia at an earlier av. age than siblings whose parents were not related. The possible role of a recessive gene in the etiology of leukemia among siblings is discussed.

70-2606 EPIDEMIOLOGY OF HODGKIN'S DISEASE. (Ger.) Dörken, H. (Univ. 1st Med. Clin., Hamburg, Germany). Arch. Geschwulstforsch. 34(4):322-335, 1969.

Evaluation of death certificates (1964/1965) revealed a mortality rate of 2.6/100,000 for males and 2.2/100,000 for females in Hamburg, 2.0 and 1.5, resp., in Schleswig-Holstein and 1.6 and 1.4, resp., in Lower Saxony. Analysis of autopsy records (1946-1964) revealed no increase in frequency (percentage of autopsies) since 1946, but high figures (1.0-1.2%) were seen for males between 1952-1956. The age distribution of 354 histologically confirmed cases in Northern Germany (199 male, 155 female) showed the typical bimodality and, in addition, a "pre-peak" of frequency between ages 1-11 yr., with a male:female ratio of 3:1. For all age groups, the male:female ratio was 1.5:1 (compared to 2.0:1 in Finland and Czechoslovakia). An increased frequency was noted in rural areas, especially among younger males (no other details), and among the higher socio-economic classes. First manifestations of the disease occurred most frequently during the winter and in some cases were preceded by infectious mononucleosis (no other details).

70-2607 PATHOLOGY AND CLASSIFICATION OF MALIGNANT LYMPHOMAS. (Ger.) Lennert, K. (U. Kiel Path. Inst., Germany). Trans. Soc. Path. Jap. 58(44):37-43, 1969.

In Schleswig-Holstein (northern Germany), a study of all lymph node biopsies reported during 1964-1966 (inclusive) indicated annual incidence rates/100,000 of 1.98 for Hodgkin's disease, 0.48 for reticulum cell sarcoma, 0.25 for lymphosarcoma, 0.27 for Brill-Symmers' lymphoma, 0.04 for Waldenström's macroglobulinemia, 0.01 for multiple myeloma, 0.01 for histiocytosis X, and 0.15 for malignant lymphomas which could not be classified. The incidence of the nodular, sclerosing form of Hodgkin's disease peaked in the 20-29-yr. age group; that of paraneoplasia for 0-50 yr., and that of Hodgkin's sarcoma for 50-90 yr. The incidence of "mixed type" Hodgkin's disease showed 2 peaks, in the 20-29 yr. and 70-79 yr. age groups.

-2608 CLINICO-PATHOLOGICAL STUDY OF MALIGNANT LYMPHOMA IN JAMAICA. (E.) Talerma, (Wytemaweg 2a, Rotterdam, Netherlands). Brit. Cancer 24(1):37-47, 1970.

om 1958-1966 (inclusive), 260 malignant lymphomas were found (and histologically confirmed) in Jamaica, comprising about 3% of all malignant tumors. The ethnic distribution of the pts. was similar to that of the total population. The distribution of types of tumor was: Hodgkin's disease, 50.9%; lymphosarcoma, 33%; reticulum cell sarcoma, 14.2%; giant follicular lymphoma, 1.9%. No Burkitt lymphomas were noted. This distribution pattern was similar to those reported in Europe and North America, except for the small proportion of giant follicular lymphomas, which differed from the patterns seen in Africa among Negroes in the absence of Burkitt's lymphoma and the greater frequency of Hodgkin's disease.

7-2609 BURKITT'S LYMPHOMA AND SICKLE CELL TRAIT. (E.) Pike, M. C. (Radcliffe Infirmary, Oxford, England), R. H. Morrow, A. Kuule and J. Mafigiri. Brit. J. Prev. Soc. Med. 21(1):39-41, 1970.

Hemoglobin electrophoretic patterns were determined in 36 pts. with Burkitt's lymphoma presenting at the Mulago Hospital, Kampala, Uganda and in matched unrelated controls of the same age, sex, tribe and place of residence in a study of the relation of Burkitt's lymphoma to sickle cell trait (AS hemoglobin). Of the 10 possible hemoglobin electrophoretic combinations, 4 are uninformative, 3 suggest AS is protective against tumor development and 3 show evidence against AS being protective. Although some support was found for the protective hypothesis, the results were not statistically significant. It is estimated that a larger series (150 pts. and their controls) is needed to test the hypothesis.

7-2610 CHILDHOOD ABDOMINAL LYMPHOMA IN ISRAEL. (E.) Hulan, N. (Govt. Hosp., Tel-Hashomer, Israel), B. Ramot and W. Sheehan. Israel J. Med. Sci. 6(2):246-252, 1970.

Cases of abdominal lymphoma at Tel-Hashomer Hospital from 1960-1967 were examined for those children under 14 yr. with no peripheral or mediastinal lymphadenopathy. Analysis of the 16 pts. (12 males, 4 females; 9 Jews, 6 Arabs and 1 Caucasian girl, ranging from 2.5-7 yr. old) showed a peak at 3.5-4 yr. Complications included testicular and retrobulbar involvement, loosening of teeth and maxillary swelling. Bone marrow infiltration or leukemic transformation were not seen. Tumors were classified as definite Burkitt's lymphoma (1), equivocal Burkitt's lymphoma (5), lymphosarcoma (5) or reticulum cell sarcoma (5). Of particular interest is the high frequency of abdominal

lymphoma among Arabs and Jewish children of North African or Middle Eastern ancestry, as opposed to Jewish children of European ancestry.

70-2611 STATISTICAL ANALYSIS OF CYTOGENETIC DATA IN CERVICAL NEOPLASIA. (E.) Cellier, K. M., J. A. Kirkland (Queen Elizabeth Hosp., Woodville, Australia) and M. A. Stanley. J. Nat. Cancer Inst. 44(6):1221-1230, 1970.

Chromosome counts were determined for 156 pts. with preinvasive or invasive carcinoma of the cervix, and a statistical analysis of their distribution and ploidy classification was made. Carcinomas were classified as being combinations of diploid (2n), triploid (3n), tetraploid (4n) or quintuploid (5n) chromosomes. A change of chromosome count distribution was seen as carcinoma in situ progressed to invasive carcinoma. For example, the 2n-3n-4n group changed to 3n dominance for that same class or to 2n dominance for the 2n-3n or 2n-4n classification. Carcinomas in situ classified as 3n-4n-5n counts were not found in invasive carcinomas. It is suggested that certain components of the chromosome population are responsible for potential neoplastic invasion and response to therapy.

70-2612 A STUDY OF FREE RADICALS OCCURRING IN TUMOROUS FEMALE BREAST TISSUE AND THEIR IMPLICATION TO DETECTION. (E.) Wallace, J. D. (Jefferson Med. Coll. Hosp., Philadelphia, Pa.), D. H. Driscoll, C. G. Kalomiris and A. Neaves. Cancer 25(5):1087-1090, 1970.

Biopsy and mastectomy specimens from 152 pts. with histological diagnoses of cancer (63) or benign lesions (89) of the breast were analyzed for free radical (FR) content. The smaller cancers showed higher FR levels than the larger tumors. A theoretical curve of the dynamic variation in FR content, as a function of tumor doubling, indicated that peak activity probably occurs at about 20 doublings (corresponding to a tumor of about 0.1 cm). As neither palpation nor mammography permit routine detection of tumors in this size range, it is suggested that, of the methods currently under study, thermography be used.

70-2613 RANDOM WALK AND THE SPREAD OF CANCER. (E.) Blumenson, L. E. (Roswell Park Mem. Inst., Buffalo, N. Y.). J. Theor. Biol. 27(2):273-290, 1970.

A mathematical model of the relationship between the "visible" and "invisible" spread of cancer, and the movements of the constituent cells of the tumor, is described. The relevance of the distinction between "visible" and "invisible" tumor spread for surgical treatment is examined, with reference to the geometry of uterine cancer.

The effects on the spread of cancer, of movements of the tumor cell in the intercellular spaces and in the small blood vessels, are examined by computer pictures generated from the mathematical model.

70-2614 THE KINETICS OF CELLULAR PROLIFERATION IN NORMAL AND MALIGNANT TISSUES. XI. ESTIMATION OF DNA SYNTHESIS TIME IN HUMAN TISSUES. (E.) Fabrikant, J. I. (Johns Hopkins U., Baltimore, Md.). Radiology 95(3):691-693, 1970.

A method is described for estimating the duration of the DNA-synthetic stage of the cell cycle, using a double-labeling method (^3H -, ^{14}C -thymidine). Specimens from 13 pts. with cancer of the larynx, trachea, bronchus and esophagus were studied. The DNA-synthetic period was 18.8-25.4 hours in malignant tumor cells, compared to 11.6-16.9 hours for benign tumor cells; the potential tissue doubling times were 214.8-260.6 and 120.0-168.2 hours, resp.

70-2615 GROWTH-RATE ANALYSIS OF EXPERIMENTAL TUMORS. A SYSTEMATIC METHOD. (E.) Meyer, J. A. (750 E. Adams St., Syracuse, N. Y.). Arch. Surg. (Chicago) 99(5):655-659, 1969.

A simplified method is presented for analysis and comparison of growth rates of experimental tumors, based on the concept of exponential growth. Growth rates are expressed as increments in log diameter per unit time, or $(\Delta \log D)/t$; this index defines the slope of the regression line for the interval between measurements. This method was applied to primary human peripheral bronchogenic carcinomas and Walker 256 carcinoma in rats.

70-2616 BODY WEIGHT AND MAMMARY GLAND PROLIFERATION PATTERNS. (E.) Sutton, H. (Argonne Nat. Lab., Argonne, Ill.) and K. Suhrbier. Argonne Nat. Lab. Ann. Rep. ANL-7535:32-34, 1968.

Body wt. and mammary gland proliferation patterns were studied in cycling female 61-65-day-old Charles River rats (divided into 3 wt. classes) 1 hour after i.v. inj. with 1 $\mu\text{C/g}$ body wt. of 0.36 C/mM ^3H -thymidine (^3T). Results showed body wt. was related to mammary gland size and gland growth. All 3 wt. classes showed qualitatively the same uptake pattern of ^3T with peaking at the metestrus stage of the estrus cycle. Although the medium-wt. class had proportionally the largest glands, DNA specific activity studies demonstrated they were growing least actively. The light-wt. body class had the largest growth rate and smallest glands, while the heavy-wt. class had an intermediate gland size and growth rate.

70-2617 MITOTIC CIRCADIAN RHYTHM IN A FAST-GROWING AND A SLOW-GROWING HEPATOMA: MITOTIC RHYTHM IN HEPATOMAS. (E.) Echave Llanos, J. M. (La Plata Nat. U. Inst. Embryol., Argentina) and R. E. Nash. J. Nat. Cancer Inst. 44(3):581-585, 1970.

The existence of a circadian rhythm was demonstrated in an undifferentiated fast-growing hepatoma (SS1K) and a differentiated slow-growing hepatoma (SS1H) maintained by grafting into 8-week-old male C3H/S mice. These tumors are 2 different sublines of a spontaneous hepatoma originally transplanted into C3H/StWi mice. During the dark period, mitotic activity was significantly greater for SS1K than for SS1H but no differences were noted during the light period. In these 2 hepatomas the mitotic activity reached a max. later than in normal livers of young C3H/S male mice. Variations in the mitotic activity in SS1H hepatomas were about the same as those in normal mouse liver while variations in the SS1K hepatoma were considerably smaller than in normal mouse liver and in the SS1H hepatoma. The circadian rhythm in mitotic activity noted in these hepatomas could be due to circadian variations in epinephrine release or glucocorticoid secretion. The greater response of the SS1H hepatoma to factors controlling circadian rhythm would explain the greater variations in its mitotic activity which approached those in normal liver.

70-2618 DIFFERENTIAL GROWTH OF HEPATOMA-SUSCEPTIBLE LIVER INDUCED BY GENE X GENOME INTERACTION. (E.) Wolff, G. L. (Inst. Cancer Res., Philadelphia, Pa.). Cancer Res. 30(6):1722-1725, 1970.

Spontaneous hepatoma incidence and the mean numbers of hepatomas/liver were greater in yellow C3H(C3H x YS) and C3H(C3H x VY) first-backcross generation, and yellow (C3H x YS)F₁ hybrid male mice, than in mice of the corresponding nonyellow strains. The lethal yellow (AY) and viable yellow (AVY) genes (in inbred mice of strains YS/ChWf and VY/Wf, resp.) were combined as F₁ hybrids with a hepatoma-susceptible genome (C3H/HeN1cr) and 2 hepatoma-resistant genomes (C57BL/6JN1cr and BALB/cAnN1cr). At age 4-16 weeks, the proportionate liver wt. was greater in the highly hepatoma-susceptible yellow C3H F₁ mice than in F₁ hybrids of the hepatoma-resistant strains (hybrids of BALB/c and C57BL/6 mice); this difference was not seen between nonyellow mice of the hepatoma-susceptible and -resistant genotypes. The nonyellow hybrids showed an age-related decrease in relative liver wt., but the yellow hybrid mice did not. It is suggested that the basis for spontaneous hepatoma susceptibility may be found in the strain-specific metabolic pattern of the liver, and that the AY and AVY genes affect a specific metabolic

threshold, involved in both normal growth regulation and hepatoma formation.

2619 GENETIC INFLUENCES ON RESPONSE TO CASTRATION OF LIVER GROWTH AND HEPATOMA FORMATION. (E.) Wolff, G. L. (Inst. Cancer Res., Philadelphia, Pa.). Cancer Res. 30(6):26-1730, 1970.

Effects of oophorectomy (oos.) or orchiectomy (orx.) on liver growth and hepatoma formation were studied in mice of several genotypes, including mice carrying the lethal yellow (AY) gene and nonyellow (a/a) mice. In male AY/a and AY/ChWf (a/a) mice, orx. reduced the water content of the livers and increased the fat content of the carcass, but not of the liver. A similar response to oos. was noted in females of these genotypes. Liver wt. was reduced after orx. in all nonyellow F₁ hybrids carrying the VY strain genome, but in only 1 yellow (AVY/A)F₁ hybrid class (strain BALB/c x VY). The YS genome apparently eliminated this response in male F₁ hybrids carrying 2 hepatoma-resistant genomes (BALB/c or C57BL/6). Liver wt. gain was retarded by orx. in the BALB/c and C57BL/6 mice, but not in males of a hepatoma-susceptible strain (C3H). It is suggested that orx. or oos. affects liver growth by altering the hormonal balance, but not directly by reducing the levels of sex hormones.

2620 STIMULATION OF GROWTH OF TRANSPLANTABLE TUMORS BY GENES WHICH PROMOTE SPONTANEOUS TUMOR DEVELOPMENT. (E.) Wolff, G. L. (Inst. Cancer Res., Philadelphia, Pa.). Cancer Res. 30(6):1731-1735, 1970.

Inbred yellow AY/a YS/ChWf and AVY/a VY/Wf mice, the growth of an allogeneic tumor (Sarcoma 3) was greater than in siblings of the non-

yellow (aa) genotype, suggesting that the tumor-stimulating effect of the lethal yellow (AY) or viable yellow (AVY) genotypes is of a systemic nature. This effect might be mediated by an increased free sulfhydryl:disulfide ratio, altering the animal's metabolic pattern toward increased anabolic activity.

70-2621 INCIDENCE AND PROGNOSIS OF ENDOMETRIAL CARCINOMA BY HISTOLOGIC GRADE AND EXTENT. (E.) Ng, A. B. P. (Case Western Reserve U. Hosps., Cleveland, Ohio) and J. W. Reagan. Obstet. Gynec. 35(3):437-443, 1970.

70-2622 CARCINOMA OF THE COLON AND RECTUM AT THE UNIVERSITY HOSPITAL, JAMAICA. (E.) Walrond, E. R. and R. Jordan. W. Indian Med. J. 18(3):152-160, 1969.

70-2623 INCIDENCE, MORBIDITY RATE AND MORTALITY FROM GASTRIC CARCINOMA IN SELECTED DISTRICTS OF WARSAW PROVINCE. (Pol.) Warda, B. (Oncol. Inst., Warsaw). Nowotwory 20(1):55-60, 1970.

70-2624 PROPHYLACTIC EXAMINATION OF WOMEN IN THE BIALYSTOK PROVINCE FOR DETECTION OF CANCER OF THE UTERINE CERVIX. (Pol.) Soszka, S. (ul. M. Curie Skłodowskiej 24a, Białystok, Poland). Ginek. Pol. 41(1):79-86, 1970.

70-2625 LEUKAEMIA AND THE RHEUMATIC DISEASES. (E.) Leavesley, G. M., L. Dougan (Cancer Council Western Australia, West Perth) and H. J. Woodliff. Med. J. Aust. 2(16):799-800, 1969.

See also abstract nos: 2119, 2122, 2125, 2126, 2127, 2133, 2134, 2135, 2136, 2137, 2138, 2139, 2164, 2166, 2167, 2168, 2169, 2173, 2228, 2319, 2320, 2321, 2382, 2470, 2494, 2650

- 70-2626 IMMUNOCYTOLOGY OF CANCER. (E.) Davidsohn, I. (Chicago Med. Sch. Univ. Health Sci., Ill.) and L. Y. Ni. Acta Cytol. (Balt.) 14(5):276-282, 1970.

The mixed cell agglutination reaction (MCAR) test was used to determine an association between malignancy and the absence or presence of A, B and H antigens. Blood type was accounted for, and connective tissue and blood vessels were used as the negative and positive controls, resp. Lung studies were made involving the normal mucosa and submucosa of the bronchus, benign lesions such as squamous cell metaplasia and dysplasia, squamous cell carcinoma, adenocarcinoma, oat cell carcinoma and anaplastic carcinoma. Positive MCAR results were obtained for normal, hyperplastic, metaplastic and dysplastic bronchial epithelia; over 90% of the bronchogenic carcinomas had a negative MCAR. Isoantigens were not seen in 50/166 pts. with metastatic bronchial carcinoma, or in all the distant metastases. It is concluded that loss of tissue isoantigens precedes metastasis; thus, in cases of carcinoma, negative results indicate a possible development of metastases.

- 70-2627 THE FUNCTION OF THE IMMUNE RESPONSE IN TUMOUR GROWTH AND ITS GENETICAL REGULATION. A NEW HYPOTHESIS. (E.) Spärck, J. V. (State Serum Inst. Immun. Lab., Copenhagen). Acta Path. Microbiol. Scand. 77(1):1-23, 1969.

Inbred C3H mice received s.c. primary spontaneous mammary carcinoma transplants from syngeneic (C3H) or allogeneic (DBA) donors, and received immunosuppressive treatment with whole-body irradiation or cortisone inj. This immunosuppression reduced tumor growth in cases where donor and host were of the same genotype. In contrast, a prolonged persistence of tumor before final regression occurred in donor-host combinations with genetic differences; thus, tumor growth is not a function of defective host immunity. To study how the host system contributes to tumor growth, the antigenic composition of tumors which developed following transplantation to chimeric or hybrid recipients, was studied. The tumors acquired the properties of the host. It is suggested that tumor formation is a reaction phenomenon, where a particular type of inflammatory proliferation of host mesenchyme is transformed into cancerous structures.

- 70-2628 NEOPLASTIC CONVERSION AND CHROMOSOMAL CHARACTERISTICS OF RAT EMBRYO CELLS IN VITRO. Jackson, J. L. (NCI, Bethesda, Md.), K. K. Sanford and T. B. Dunn. J. Nat. Cancer Inst. 45(1):11-23, 1970.

ALB/N rat embryo cells, presumably free of murine leukemia virus, were grown on chemically defined

medium supplemented with horse serum (HS) or fetal calf serum (FCS). Within 412 days, 3/3 cultures grown on HS-supplemented medium and 1/2 lines grown on FCS-supplemented medium, produced sarcomas when inj. intraocularly or i.m. into adult ALB/N rats. Tumor latent periods were shorter with cells grown on HS medium, and tumors were produced after shorter periods of cultivation when the cells were frozen and then thawed. Chromosome studies of subcultured lines revealed that after an initial period of karyotypic stability (61-110 days), extensive chromosome changes occurred long before the cells were able to induce tumors. However, no specific chromosomal changes were associated with the ability of these cell lines to induce rat tumors. These findings neither support nor refute the possibility that chromosomal changes are responsible for tumor induction.

- 70-2629 SEQUENTIAL CYTOGENETIC CHANGES IN THE DEVELOPMENT OF METASTATIC THYROID CARCINOMA. Beierwaltes, W. H. and A. A. Al-Saadi. Pp. 319-344, in Thyroid Neoplasia, Young, S. and D. R. Inman (Eds.). Academic Press, London, 1968, 470 pp.

Iodine deficiency (ID)-induced hyperplastic goiters from male and female Fischer rats, transplanted s.c. into ID, ¹³¹I-thyroidectomized rats, grew into tumors of 3 stages of malignancy: thyroid-stimulating hormone (TSH)-dependent adenocarcinomas or follicular carcinomas; "transitional" follicular and papillary carcinomas; and autonomous anaplastic carcinomas with widespread metastases. Tumor growth rates increased with increasing tumor autonomy. All TSH-dependent tumors progressed to the intermediate stage (sometimes to the autonomous stage) upon serial transplantation. Numerical and structural chromosomal abnormalities (CA) of 3 different patterns were seen in the ID-induced goiters. The transplantability of the goiters and the frequency of CA increased with increasing durations of ID. The frequency of CA also increased according to the malignancy of the tumors. Since each tumor showed the same pattern of CA as its parent transplanted goiter, it is suggested that the tumors developed from a single cell or clone of the goiter. Loss of 1 chromosome from pair #15 seemed to be essential for tumor progression from TSH dependence to autonomy; it is suggested that chromosome #15 may carry genetic information concerned with thyroid growth regulation in the Fischer rat. Thyroidectomy specimens from 20 pts. with hyperplastic thyroid diseases (including 2 carcinomas) also showed significant aneuploidy and many structural CA of various types.

- 70-2630 KARYOLOGICAL STUDIES ON TWO HeLa LINES. (E.) Ghosh, I. (U. Heidelberg Inst. Exp. Cancer Res., Germany) and S. Ghosh. Z. Krebsforsch. 74(1):103-109, 1970.

Chromosome studies were made on 2 lines of HeLa cells which originated from the same stock but were grown under different conditions. One line, a "monolayer" culture, had a stemline chromosome number of 69 while the other line, a "clot" culture, had a stemline with 74 chromosomes. Although the monolayer line had a triploid chromosome number, its karyotype had 1 extra C and 2 extra D chromosomes, but lacked 2 F chromosomes and 1 G chromosome. The "clot" line, which had 5 chromosomes more than the normal triploid number, had 4 extra C chromosomes and 1 extra G chromosome.

- 70-2631 CLONING OF HUMAN HEMATOPOIETIC CELL LINES. (E.) Imamura, T. (Nagoya U. Sch. Med., Japan), C. C. Huang, J. Minowada, M. Takahashi and G. E. Moore. J. Nat. Cancer Inst. 44(4):845-854, 1970.

Cloning characteristics in soft agar of 28 human hematopoietic cell lines were studied; 10 were derived from normal subjects, 12 from pts. with various leukemias, myeloma, melanoma or lymphoma, and 6 from pts. with nonmalignant diseases such as rheumatic fever or infectious mononucleosis. All cell lines derived from the buffy coat of normal subjects and those from pts. with nonmalignant diseases had cloning efficiencies of less than 6% and developed no macroscopic colonies. Intermediate cloning efficiencies of 12-36% and some macroscopic colonies were observed with 4/12 cell lines from pts. with malignancies; 7 lines appeared normal and were probably derived from normal blood cells. One cell line from a pt. with multiple myeloma had a cloning efficiency of about 60%. In general, intermediate and high cloning efficiencies were correlated with abnormal chromosome constitutions. With the exception of 1 cell line from a pt. with acute lymphocytic leukemia, low cloning efficiencies and an absence of macroscopic colonies were characteristic of cell lines with a normal diploid chromosome pattern. Herpes-type virus (leukovirus) particles were seen in 11/23 cell lines, involving no more 1-3% of the cells. No correlation was observed between cloning efficiency and the presence or absence of these virus particles. Lines with high or intermediate cloning efficiencies could be subcultured with far fewer cells than lines with low cloning efficiencies. These cloned sublines were similar in cloning efficiency, chromosome constitution and immunoglobulin production to the parental cell lines. It is concluded that the cloning efficiency of human hematopoietic cell lines may be regarded as an indirect indicator of the relative normality or malignancy of the cells.

- 70-2632 SOME PROPERTIES OF A NEW EPITHELIAL CELL LINE OF HUMAN ORIGIN. (E.) Sykes, J. A. (Southern California Cancer Ctr., Los

Angeles), J. Whitescarver, P. Jernstrom, J. F. Nolan and P. Byatt. J. Nat. Cancer Inst. 45(1):107-122, 1970.

An epithelial human cell line (ME-180) was derived from omental metastases of a rapidly spreading cervical carcinoma. Cellular chromosome numbers ranged from 48-130 and there was evidence of chromosomal rearrangements characteristic of cell transformation, including fragmentations and dicentric. Marker chromosomes were occasionally observed, but these formed no stemline. This line was classified as a heteroploid with a subtriploid mode and unstable karyotype. ME-180 cells showed a massive and rapid cytopathic effect (CPE) with Coxsackie virus A-9, but not with A-11 or A-13. Characteristic enterovirus cytopathology was seen with all Coxsackie B viruses with the exception of B-1. ECHO viruses 1, 3, 7, 9 and 11 all induced a rapid and gross CPE. ME-180 cells formed carrier cultures with some viruses, especially influenza and other myxoviruses.

- 70-2633 GUINEA PIG LEUKEMIA L₂C: CHARACTERIZATION OF CHROMOSOMES AND ATTEMPTS TO DEMONSTRATE ANTIGENICITY. (E.) Wepsic, H. P. (NCI, Bethesda, Md.), B. Zbar, J. Whang-Peng, T. Borsos and H. J. Rapp. J. Nat. Cancer Inst. 45(1):99-105, 1970.

Unsuccessful attempts were made to immunize Sewall-Wright inbred strain-2 male guinea pigs against transplantable L₂C leukemia by excision of intradermal leukemic nodules or by intradermal inj. with sublethal doses of living L₂C cells, with L₂C cells that had been placed in short-term tissue culture, or with L₂C cells from histoincompatible Hartley guinea pigs. This lack of antigenicity may be due to tolerance, spontaneous origin or inadequate testing. The chromosomal constitution of leukemic cells, studied in male and female strain-2 and Hartley guinea pigs, was of a female karyotype and did not differ with strain or sex, as would be expected if this form of leukemia were caused by a virus. These findings indicate that induction of L₂C leukemia results from proliferation of transplanted blast cells and not from release of virus from these cells.

- 70-2634 EXPERIMENTAL STUDIES ON LEUKEMIA IN GUINEA PIGS. (E.) Gross, L. (VA Hosp., Bronx, N. Y.), Y. Dreyfuss, T. Ehrenreich and L. A. Moore. Acta Haemat. (Basel) 43(4):193-209, 1970.

The L₂C strain of guinea pig leukemia was consistently transmitted to young adult strain-2 or (Hartley x strain-2)F₁ hybrids by s.c. inj. of 10-20% cell suspensions of spleen, lymph nodes and a tumor from a guinea pig with leukemia. The guinea pigs first developed

tumors at the site of inoc. followed by a rapidly progressive stem-cell leukemia. Leukemia was also induced by s.c. inj. of unfiltered plasma, but not filtered plasma, from leukemic animals. Supernatants, obtained by centrifuging cell suspensions twice, induced leukemia in young adult strain-2 guinea pigs, but supernatants from suspensions centrifuged 3 or 4 times had no effect. This may be due to the presence of leukemia cells in the former supernatants or to the relatively short observation period. Filtered tumor and spleen extracts have not induced leukemia in 79 newborn or 21 young adult guinea pigs. Electron microscope studies revealed the presence of virus particles with a fuzzy, granular outer coat in leukemic cells.

- 70-2635 PHILADELPHIA-CHROMOSOME-POSITIVE AND -NEGATIVE CHRONIC MYELOCYTIC LEUKEMIA. (E.) Ezdinli, E. Z. (Roswell Park Mem. Inst., Buffalo, N. Y.), J. E. Sokal, L. Crosswhite and A. A. Sandberg. Ann. Intern. Med. 72(2):175-182, 1970.

Chromosomal analysis of 61 pts. with typical chronic myelocytic leukemia revealed 43/61 were Philadelphia chromosome positive (Ph⁺) and 18/61 were negative (Ph⁻). Evaluation showed the Ph⁺ pts. were somewhat younger (median age, 48 yr.) as compared to Ph⁻ pts. (median age, 66 yr.) and were comprised of a male:female ratio of 21:22 as compared to 16:2 for Ph⁻ pts. Of the 61 pts., 5 women (all Ph⁺) had been treated with ionizing radiation 2-20 yr. prior to leukemia onset. WBC alkaline phosphatase was absent in the same proportion of both groups. Ph⁺ pts. were characterized by a good initial response to therapy and a variable, but substantial, period during which no clinical or hematological deterioration occurred. Ph⁻ pts. had lower platelet and WBC levels, more bone marrow and peripheral blood myeloblasts, were less likely to develop thrombocytosis or basophilia, responded poorly to chemotherapy, entered overt blastic crises early and usually died within 1 or 2 yr. of diagnosis. Karyotypic analysis furnished a subclassification of myelocytic leukemia with significant prognostic and therapeutic implications.

- 70-2636 CHROMATIN AND OTHER CYTOLOGIC INDICES IN CHRONIC LYMPHOCYTIC LEUKEMIA. (E.) Schrek, R. (VA Hosp., Hines, Ill.), W. H. Knospe and F. E. Trobaugh, Jr. J. Lab. Clin. Med. 75(2):217-224, 1970.

A quantitative method used to compare the cytology of viable lymphocytes from 60 control subjects and 36 pts. with leukemia (chronic lymphocytic or lymphosarcoma-cell), was used to determine the percentage of lymphocytes positive for chromatin masses, nucleoli and/or nuclear indentation of a specific size. Results showed chromatin and nucleolar indices for most pts. with chronic

lymphocytic leukemia (CLL) were higher than those for normals. The nuclear indentation index was usually less for leukemic than for normal lymphocytes. Data indicated that the blood lymphocytes in pts. with CLL were different from normal lymphocytes. The elevated chromatin indices in most CLL pts. indicated that leukemic lymphocytes have increased heterochromatin, increased amount of inactive DNA and an increased number of depressed genes.

- 70-2637 G-TRISOMY IN ACUTE ERYTHROLEUKEMIA. (Ger.) Khan, M. H. (Goethe U. Ctr. Intern. Med., Frankfurt a. M., Germany) and H. Martin. Klin. Wschr. 48(7):445-447, 1970.

In a 58-yr.-old man with erythroleukemia, cytogenetic studies of blood cultures showed that 86% of the cells were diploid with the normal number of chromosomes. However, cultures of bone marrow cells had a dominant cell line with 47 chromosomes; the extra chromosome was identified as a G. This pt. did not have Down's syndrome. It is suggested that the association of leukemia with G trisomy but with none of the clinical features of Down's syndrome, might result from somatic mutation of a recessive gene. Somatic mutation might also result from genetic "imbalance" caused by another carcinogenic factor.

- 70-2638 CYTOGENETIC ANALYSIS IN TWO CASES OF LYMPHOMA. COMPARISON BETWEEN LYMPHOSARCOMA AND RETICULOSARCOMA. (E.) Wisniewski, L. (2nd Clin. Obstet. Gynec., Bialystok, Warsaw, Poland) and E. Korsak. Cancer 25(5):1081-1086, 1970.

Chromosome studies were made on lymphocyte cultures from a 65-yr.-old man with lymphosarcoma and a 47-yr.-old man with reticulum cell sarcoma. Both qualitative and quantitative chromosomal aberrations were found in lymphocytes from the pt. with lymphosarcoma. The number of chromosomes varied from 44 to 49; 9% of the cells were hypodiploid and 25% were hyperdiploid. Nine marker chromosomes were found in 7 cells. Pseudodiploid karyotypes were found in 4 cells and satellite enlargement was noted. No chromosome aberrations were found in lymphocytes from the pt. with reticulum cell sarcoma.

- 70-2639 TYPE I DYSGAMMAGLOBULINEMIA, SYSTEMIC LUPUS ERYTHEMATOSUS AND LYMPHOMA. (E.) Smith, C. K. (U. Washington Sch. Med., Seattle), J. T. Cassidy and G. G. Bole. Amer. J. Med. 48(1):113-119, 1970.

Clinical, serological and pathological findings in a 63-yr.-old woman with systemic lupus erythematosus (SLE), type 1 dysgammaglobulinemia and lymphoma (the first reported concurrence of these disorders), and a review of 8 previously reported cases of SLE and lymphoma (including 1

with hypogammaglobulinemia) are presented. This pt. showed a high titer of IgM antinuclear antibodies, extensive development of extracellular hematoxylin-staining material and restricted ability to form LE cells. The cryoglobulinemia present was related mostly to IgM. Pathogenic interrelationships between connective tissue disease, immunity deficiencies and lymphoma are stressed.

2640 MOUSE MYELOMAS AND LYMPHOMAS IN CULTURE. (E.) Horibata, K. (Salk Inst. Biol. Studies, San Diego, Calif.) and A. W. Harris. Exp. Cell Res. 60(1):61-77, 1970.

Initiation, cell morphology, growth characteristics, cloning, immunoglobulin synthesis, chromosome content, tumor production and responses to thymidine, hydrocortisone and 8-azaguanine are described for 9 cell lines originating from 5 transplantable plasmacytomas of BALB/c or C3H mice and from 2 oil-induced lymphomas of BALB/c mice. Although different lines were initiated by somewhat different methods, they all grew in fortified Eagle's medium supplemented with horse serum as stationary suspension cultures with doubling times between 16-26 hours. Some of the lines were near-tetraploid and contained marker chromosomes, while others were diploid or near-diploid. With the exception of 1 lymphoma line in which the cells were pleomorphic, growing cultures consisted of spherical cells. In general, the vol. of myeloma cells was twice the vol. of lymphoma cells and, for a given cell type, doubling of the chromosome number was associated with doubling of the cell vol. Five of the myeloma lines synthesized and secreted immunoglobulin while 2 others, probably as a result of mutation, did not. Neither of the lymphoma lines secreted significant amounts of immunoglobulin, but there is preliminary evidence that they synthesized it but did not release it from the cells. All cultured cell lines initiated tumor growth in mice.

2641 FURTHER CYTOGENETICAL INVESTIGATIONS IN POLYCYTHAEMIA VERA. (E.) Lawler, D. (Roy. Marsden Hosp., London), R. E. Millard and H. E. M. Kay. Europ. J. Cancer 6(3):223-233, 1970.

Chromosome studies were made on bone marrow cells from 79 pts. with polycythemia vera. Of 33 treated pts., 4/12 female and 1/16 males had aneuploid karyotypes. All 4 of the females had 1 or more extra group C chromosomes, which involved the entire cell population in 2/4. The male lacked a Y chromosome in all of the cells examined. Of 46 pts. examined after ³²P or sulfin treatment was begun, 14 had normal karyotypes, 16 had predominantly normal cells and some cells exhibited signs of radiation damage, had clones of cells with an abnormality possibly involving group F, 5 had other major clonal

abnormalities, and 4 had gross chromosome abnormalities associated with leukemia. Another 5 treated pts. subsequently developed leukemia. The possible group F abnormality may be related to treatment.

70-2642 NEW ANIMAL FOR EXPERIMENTAL CANCER RESEARCH: Phodopus sungorus. (Rus.) Pogosiants, E. E. (Inst. Exp. Clin. Oncol., Moscow), O. I. Sokova and E. L. Prigozhina. Vop. Onkol. 16(3):90-97, 1970.

Study of 225 female and 210 male striped, hairy-footed hamsters (Phodopus sungorus campbelli) showed a high frequency of spontaneous tumors in this species (11.8% for females and 6.2% for males), which increased considerably with age. Of the 43 tumors observed in 38 hamsters (25 females and 13 males), the most common were squamous cell carcinomas of the skin (18 cases), lung tumors (9 cases), mammary tumors (9 cases, females only), and hematopoietic tumors (4 cases). Benign tumors were diagnosed in 6 cases (3 liver tumors, 1 uterine myoma, 1 skin papilloma, and keratinized cysts on the digits) and precancerous conditions in 4 (glandular hyperplasia of the liver and gastric mucosa and the beginnings of a renal adenoma and a lung tumor). Multiple tumors were found in 5 females and 6 males. Tumors developed between the ages of 8 and 31 mo. Experiments in 43 hamsters (13 females and 30 males, aged 3-8 mo.) demonstrated that urethan (dose and route unspecified) does not induce tumors in this species. Admin. of 3-methylcholanthrene (dose and route unspecified) induced local sarcomas in 4/21 hamsters. (age and sex not specified). Inj. of 7,12-dimethylbenzanthracene (0.5-2 mg) induced tumors in 21/47 surviving hamsters. Distant tumors observed in 6 cases were most likely spontaneous in origin.

70-2643 CHARACTERISTICS OF A NEW INBRED STRAIN OF MICE (PBA) WITH A HIGH TUMOR INCIDENCE: PRELIMINARY REPORT. (E.) Bailey, P. C. (Birmingham-Southern Coll., Ala.), W. B. Leach and M. W. Hartley. J. Nat. Cancer Inst. 45(1):59-73, 1970.

A new inbred strain of mouse (PBA) was developed by brother x sister matings of offspring from a single pair of albino mice. These animals developed 3 different types of neoplasms spontaneously: 100% developed plasma cell lymphomas at an av. age of 35 weeks; 74.3% of the breeding females developed primary mammary tumors at an av. age of 38 weeks; and 77% of all mice over 1 yr. old developed pulmonary adenomas. The lymphomas characteristically involved the peripheral lymph nodes and spleen, but not the liver. Enlargement of the lymph nodes was due to proliferation of mature and immature bone marrow plasma cells having Russell bodies. Serum γ -globulins were increased in

56-72% of PBA mice with lymphomas. The mammary tumors were solitary or multiple adenocarcinomas with differentiation ranging from mature glandular patterns to anaplastic sheets of pleomorphic epithelial cells. Some of these mice had wide-spread metastases. A foster-nursing experiment in which PBA females nursed C57BL/6J young indicated that a milk factor, similar to that reported by Bittner, was present. The pulmonary tumors were solitary or multiple adenomas; mammary metastases were found in 4/24 mice.

- 70-2644 SELECTIVE BREEDING FOR THYROID ^{131}I UPTAKE IN MICE. (E.) Chai, C. K. (Jackson Lab., Bar Harbor, Maine). Genetics 64(1):29-40, 1970.

Selective breeding of a hybrid mouse strain for low and high ^{131}I uptake by thyroid included studies of thyroid activity, urinary iodine excretion, protein bound iodine and thyroid wt., as well as basal metabolism, growth and maturation and response to X-irradiation. A 4-fold difference in ^{131}I uptake was seen between the high- and low-uptake lines. Other differences, considered to be a consequence of the greater uptake of iodine and of pleiotropic effects of genes, included a higher basal metabolism, earlier maturation, greater sensitivity to X-irradiation and a faster body growth rate.

- 70-2645 SEPARATION OF MALIGNANT CELLS FROM TRANSPLANTABLE RODENT TUMORS. (E.) Pretlow, T. G., II (Rutgers Med. Sch., New Brunswick, N. J.) and C. W. Boone. Exp. Molec. Path. 12(3):249-256, 1970.

Tumors were induced by inoc. of tumor cell suspensions into 5-7-week old animals. They included: transplantable melanotic melanoma from a golden Syrian hamster; melanoma S91v/La from a DBA mouse; and C57BL mouse melanoma B16. Ficoll density gradient studies were used to separate viable malignant cells from the disaggregated transplantable solid tumors. The hamster melanotic melanoma was cloned 2 times in culture; upon disaggregation, 49.5-54% of the cells were capable of converting dihydroxyphenylalanine to melanin. A purity of 89-91.5% was achieved upon concentration. The B16 and S91v/La mouse melanomas were concentrated 2.2-3.2- and 2.0-2.7-fold, resp.

- 70-2646 THE ROLE OF THE HOST MESENCHYME IN THE DEVELOPMENT OF TUMOURS AFTER TRANSPLANTATION. (E.) Spärck, J. V. (State Serum Inst. Immun. Lab., Copenhagen) and K. Gross. Acta Path. Microbiol. Scand. 77(1):24-38, 1969.

Tissue samples from the transplantation area of inbred C3H mice, inoc. s.c. 1 hour-2 weeks previously with spontaneous mammary tumors from C3H or DBA mice, were examined for changes in the morphology of connective tissue. Changes (disintegration of the inoc. tumor tissue and initial activation of host mesenchyme) occurring within 48 hours of inoc. were similar in syn-

geneic and allogeneic donor-host combinations. At 72 hours the syngeneic host continued to show further cell proliferation of the RES and tumor development, while the reactions in an allogeneic host were of a subacute inflammatory process with marked round cell infiltration leading to normal formation of granulation tissue. The apparently complete destruction of the implanted cellular material in both compatible and incompatible combinations supports the theory of tumor formation based on proliferation of primitive connective (mesenchymal) tissue.

- 70-2647 TRANSFER RNA-METHYLATING ENZYMES IN MAMMARY CARCINOMA CELLS. (E.) Turkington, R. W. (Duke U. Med. Ctr., Durham, N. C.) and M. Riddle. Cancer Res. 30(3):650-657, 1970.

Activities of enzymes which methylate transfer RNA (tRNA) were measured in cell-free extracts from homogenates of mammary carcinomas from the C3H mouse and Fischer rat and in extracts of normal mammary tissue from lactating or pregnant animals. Activity was measured by the amount of radioactivity transferred from ^{14}C -S-adenosyl-L-methionine to the individual bases of an exogenous tRNA acceptor from *Escherichia coli* K12 or yeast. Total tRNA methylating activity was markedly higher in tumor cells than in normal mammary cells. Although the amount of methylating activity in normal mammary tissue is proportional to the cellular tRNA content, elevated methylating activities in carcinoma cells were associated with reduced tRNA contents. While the activity of N^2, N^2 -guanine "dimethylase" was above the normal range for all tumors, activities of aminopurine 6-methylase in Fischer rat carcinomas and cytosine 5-methylase and guanine N^1 -methylase in spontaneous mouse carcinomas were all in the normal range. Extracts from tumor tissue formed 7-methylguanine which was not produced when normal mammary extracts were incubated with exogenous tRNA substrate. However, guanine 7-methylase was found in the liver, lung, spleen and kidney of normal mice. It is suggested that genetic information for this enzyme was activated in the cells of mammary carcinomas, apparently as a result of virus-dependent malignant transformation.

- 70-2648 INFRARED STUDIES OF ISOLATED NORMAL AND TUMOUR DNA. (E.) Webb, S. J. (U. Saskatchewan, Saskatoon, Canada) and R. Bather. Phys. Med. Biol. 15(2):271-279, 1970.

Infrared studies of isolated normal and tumor (Rous sarcoma from chicks, mouse mammary carcinoma, hamster carcinoma) DNA at different levels of relative humidity (RH) showed that tumor DNA differed from normal DNA in 2 interrelated ways; at high RH levels it was less hydrated and displayed a smaller dichroism at 1670 cm^{-1} , and it retained more water and had a greater dichroism at lower levels of RH. The observed changes in

permanently somewhere between the B and A forms of DNA. It is postulated that the ability of normal DNA to change from the B to A forms as a result of bound water movement is necessary for normal regulation of metabolic processes and, since tumor DNA seems to fail to alter its configuration in the same manner as normal DNA, normal metabolic regulation cannot occur.

0-2649 MULTIPLE MALIGNANT NEOPLASMS IN A GOLDEN HAMSTER. A CASE REPORT AND LITERATURE SURVEY. (E.), Kesterson, J. W. (Purdue U. Sch. Vet. Sci. Med., Lafayette, Ind.) and W. W. Carlton. Lab. Anim. Care 20(2, Pt.1): 220-225, 1970.

2.5-yr.-old male Syrian hamster with multiple, spontaneous malignant neoplasms (hemangioendotheliomas) involving the liver, heart, kidney, adrenal gland and spleen, as well as a pheochromocytoma metastatic to the lung, is described. The hamster was senile and in run-down condition; admin. of vitamins was necessary to offset severe hair loss. Etiology of neoplasms in hamsters, with frequent spontaneous tumors but few reports of multiple neoplasms, is still vague, but hormonal imbalance, dietary deficiency, unsuspected toxic agents and nonspecific stress are suggested as factors for the principal mechanism.

0-2650 TUMORS OF THE TESTIS IN THE MEXICAN AXOLOTL (*Ambystoma*, OR *Siredon*, *exicanum*). Humphrey, R. R. Pp. 220-228 in Biology of Amphibian Tumors, Mizell, M. (Ed.). Springer-Verlag, New York, 1969, 484 pp. Recent Results Cancer Res., Special Suppl.).

Benign tumors of the testis occurred in 16/497 (3.2%) Mexican axolotls (10/16 were definitive and 6/10 were incipient tumors). Tumors arose from the proliferation of the spermatogonia and associated indifferent cells at the subperitoneal ends of a group of tubules, usually those of a testicular lobe in which tubules were regenerated after emptying. In males developing large tumors, regeneration of normal tubules was inhibited, new spermatogonia resulting from mitoses degenerated and the entire nontumorous portions of both testes became reduced to rudiments. Males with definitive tumors and vestigial testes produced sufficient androgens to maintain an active state in the glands of the cloaca and the epithelium of the ductus deferens. The loss of the usual connection of the tubules to the ducts may be of etiologic significance. A genetic influence was suspected; 1 family group with 7 affected animals in 5 generations was found. The possible role of a virus is discussed, but no conclusions could be drawn.

-2651 ADRENAL MEDULLARY CALCITONIN-LIKE FACTOR: A KEY TO MULTIPLE ENDOCRINE NEOPLASIA, TYPE 2? (E.) Kaplan, E. L. (Michael Reese Hosp. Rothschild Lab. Surg. Res., Chicago, Ill.), C. D. Arnaud, B. J. Hill and G. W. Peskin. Surgery 68(1):146-149, 1970.

A calcitonin-like factor was derived from the porcine adrenal medulla, but little or none was extractable from the adrenal cortex. Since an equal wt. of adrenal medulla contains 7-28% as much calcitonin-like activity as does thyroid from the same animals, it is indicated that C cells, which produce calcitonin, are of neural-crest origin and that extrathyroidal calcitonin may be of significant importance in some species of animals. The demonstration of a calcitonin-like factor in the porcine medulla supports the hypothesis that the multiple endocrine neoplasia (Type 2) syndrome may be a systemic disorder of neuroectodermal cells.

70-2652 DAILY VARIATION OF BODY TEMPERATURE, LIVER CATALASE ACTIVITY, AND PLASMA IRON CONCENTRATION IN NORMAL AND TUMOR-BEARING RATS. (E.) Kampschmidt, R. F. (Samuel Roberts Noble Found. Inc., Ardmore, Okla.) and H. F. Upchurch. Proc. Soc. Exp. Biol. Med. 134(2): 527-529, 1970.

Normal rats and rats bearing transplanted Walker 256 carcinosarcoma or 3-methylcholanthrene (MC; 20 mg, i.m.)-induced sarcoma of the Holtzman and Fischer strains, resp., were compared for variations in body temperature, liver catalase activity and plasma iron conc. A 24-hour rhythm was seen for all 3 factors in the normal rats, whereas cycles were altered in tumor-bearing rats. Alterations in the tumor-bearing rats included a lower-than-normal body temperature peaking shortly after dark, a slightly lower plasma iron conc. reaching a minimum 4 hours later than in normal rats and a decreased liver catalase activity, especially during the dark cycle. It is concluded that comparisons of normal and tumor-bearing rats should be made at the appropriate point in their daily cycles.

70-2653 CAROTID BODY TUMORS: FAMILIAL AND BILATERAL. (E.) Wilson, H. (U. Tennessee, Memphis), Ann. Surg. 171(6):843-848, 1970.

Large bilateral carotid body (CB) tumors (chemodectomas) were tentatively diagnosed in a 65-yr.-old man. Surgery for CB tumors had been previously performed in 2/3 brothers, 2/2 sisters and the daughter of the proband. Of his brothers, 1/2 had bilateral CB tumors occurring at different times, and his son also had a CB tumor. A nephew (son of the unaffected brother) also had a CB tumor. Features in diagnosis and surgical treatment of CB tumors are reported. It is concluded that there is a familial tendency for CB tumors to be bilateral. Several previously reported familial cases are included in the discussion.

70-2654 FAMILIAL POLYPOSIS COLI ASSOCIATED WITH EXTRACOLONIC ABNORMALITIES. (E.) Parks, T. G. (St. Mark's Hosp., London), H. J. R. Bussey and H. E. Lockhart-Mummery. Gut 11(4):323-329, 1970.

Familial polyposis coli (PC) was diagnosed or suspected in 15/46 individuals through 3 generations of a family. Of these 15, extracolonic abnormalities are described in 4 case histories (3 brothers and the daughter of 1); 4 others, who have developed adenomas, have not as yet received surgical treatment. Unusual features observed in conjunction with PC include the symptoms of Gardner's syndrome and the development of a neural tumor possibly associated with Turcot's syndrome.

- 70-2655 FAMILIAL SARCOMA OF BONE IN A POLYPOSIS COLI FAMILY. (E.) Hoffmann, D. C. (St. George's Hosp., London) and B. N. Brooke. Dis. Colon Rectum 13(2):119-120, 1970.

Osteogenic sarcoma or fibrosarcoma-chondrosarcoma of the bone developed in a mother and son of a family in which 6/35 members developed polyposis coli (PC). One member also had multiple sebaceous cysts. The mother and son both underwent radiation therapy and died with metastases to the lung within 18 and 5 mo. of diagnosis, resp. As autopsy was not performed in either case, intestinal evidence of PC could not be demonstrated.

- 70-2656 A POSSIBLE RELATIONSHIP OF NEUROBLASTOMA TO VON RECKLINGHAUSEN'S DISEASE. (E.) Bolande, R. P. (Child. Hosp., Akron, Ohio) and W. F. Towler. Cancer 26(1):162-175, 1970.

From a histological study of 46 neurofibromas found in 19 pts. (aged 3-20 yr.) with von Recklinghausen's disease and a review of the literature, it is hypothesized that in some cases neurofibromatosis may be derived from disseminated neuroblastoma of aberrantly migrating neural crest cells, particularly when congenital neuroblastomas are associated with multiple regressing skin and visceral metastases. In 6 cases of neurofibromatosis, ganglion cells or neuroblastic cell elements were found within neurofibromatous tissue. A comparison was made between von Recklinghausen's neurofibromas and 7 isolated ganglioneuromas in children (aged 4-12 yr.) with no family histories of von Recklinghausen's disease, neuroblastoma or ganglioneuroma. Histological and ultrastructural features were similar in these 2 types of tumors. The only distinction was the prominence of lymphoid aggregates in ganglioneuromas.

- 70-2657 MALHERBE'S CALCIFYING EPITHELIOMA WITH SIGNS OF MALIGNANT TRANSFORMATION. (Rus.) Prandetskii, A. P. (Kirov Milit. Med. Acad., Leningrad, USSR) and A. K. Iuzvinkevich. Ark. Pat. (12):64-66, 1969.

A 52-yr.-old woman who developed a Malherbe epithelioma on the hip, several mo. after bruising it, is described. In contrast to most epitheliomas of this type, which are considered

benign, this tumor contained areas of tumor tissue consisting of cells with hyperchromic nuclei, in many of which mitosis was evident. These tumor cells were infiltrating into the s.c. tissue.

- 70-2658 PRIMARY CARCINOMA IN AN ARTIFICIAL VAGINA. (E.) Ramming, K. P., Y. H. Pilch, R. D. Powell, Jr. (NCI, Bethesda, Md.) and A. S. Ketcham. Amer. J. Surg. 120(July):108-112, 1970.

Pelvic exenteration, followed by construction of an artificial vagina (modification of the McIndoe method; split thickness skin grafts held in place in a surgically created perineal defect by a stent) was performed on a 34-yr.-old woman with epidermoid carcinoma of the cervix. About 4.5 yr. after vaginoplasty, submucous resection of the posterior vagina was performed and examination of the excised specimen revealed invasive epidermoid carcinoma. This is the second reported case of primary carcinoma arising in an artificial vagina. The possibility that potential for malignant transformation can be regionally conferred to grafted skin is considered.

- 70-2659 DYSGERMINOMA OF THE OVARIES IN SISTERS. (Slovak) Maňka, I. (Inst. Oncol., Bratislava, Czechoslovakia) and E. Klaber. Bratisl. Lek. Listy 53(5):581-583, 1970.

Two sisters (ages 14 and 16 yr.) who underwent surgery for bilateral ovarian dysgerminomas are described. In both cases the right ovary appeared normal on gross examination but, on histological examination, proved to be composed of large clear cells arranged in thick layers. It is recommended that biopsies be taken and histological examinations be made during surgery for ovarian dysgerminomas.

- 70-2660 COMPARISON OF CYTOLOGIC FINDINGS IN PATIENTS WITH TRANSITIONAL CELL CARCINOMA AND BENIGN UROLOGIC DISEASES. (E.) Kalnins, Z. A. (Wake Forest U. Bowman Gray Sch. Med., Winston-Salem, N. C.), A. L. Rhyne, R. P. Morehead and B. J. Carter. Acta Cytol. (Balt.) 14(5):243-248, 1970.

Criteria for the identification of transitional cell carcinomas of the bladder and renal pelvis, using correlation and stepwise regression, were developed by computer analysis on data from cytological studies of urine specimens from 20 pts. with proven cancer and 10 pts. with benign diseases of the bladder and kidney. Of the 24 cytological characteristics studied, 9 were particularly typical of malignancy and 3 of benign diseases. The characteristic most significantly correlated with malignancy was irregularly shaped nucleoli. A combination of irregularly shaped nucleoli, unevenly distributed and coarsely

granular chromatin, and multinucleated cells correlated well with transitional cell carcinoma.

2661 SEX CHROMATIN IN UTERINE CARCINOMA.

(Rus.) Zhelezov, B. I. (All-Union Sci. Res. Inst. Obstet. Gynec., Moscow) and I. Kondrikov. Akush. Ginek. (Moskva) 45(3): 7, 1969.

2662 CHROMOSOMES OF 14 HEMATOPOIETIC CELL LINES DERIVED FROM PERIPHERAL BLOOD OF PERSONS WITH AND WITHOUT CHROMOSOME ANOMALIES.

(E.) Huang, C. C. (Roswell Park Mem. Inst., Springville, N.Y.) and G. E. Moore. J. Nat. Cancer Inst. 43(5):1119-1128, 1968.

2663 CHROMOSOMES AND CLONING EFFICIENCIES OF HEMATOPOIETIC CELL LINES DERIVED FROM PATIENTS WITH LEUKEMIA, MELANOMA, MYELOMA, AND BURKITT LYMPHOMA. (E.) Huang, C. C. (Roswell Park Mem. Inst., Springville, N.Y.), T. Imamura and G. E. Moore. J. Nat. Cancer Inst. 43(5): 29-1146, 1968.

2664 CHROMOSOMES OF HETERO- AND HOMOTRANSPLANTED HUMAN AND HAMSTER TUMORS. (Ger.) Lampert, F. (U. Erlangen-Nurnberg, Erlangen, Germany), P. Karsch and D. M. Goldenberg. ch. Geschwulstforsch. 32(4):309-321, 1968.

2665 CHROMOSOME FEATURE OF YOSHIDA ASCITES SARCOMA TRANSPLANTED IN VARIOUS STRAINS OF RATS. (Jap.) Sasaoka, I. (Gifu U. Sch. Med., Gifu, Japan), C. Shibuya, H. Irino and K. Hayashi. ta Sch. Med. Gifu 17(1):93-102, 1969.

2666 TRANSITION OF CHRONIC ULCERS OF THE LOWER EXTREMITIES INTO CANCER. (Rus.)

Sakharov, I. I. (Izhevsk Med. Inst. Gen. Surg. Clin., USSR), G. I. Volkov and V. P. Efimov. Klin. Khir. (12):51-52, 1969.

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70-2668 INVESTIGATIONS ON THE TRANSFORMATION OF FIBROADENOMA OF THE BREAST INTO MALIGNANT CYSTOSARCOMA PHYLLODES. (E.) Zółtowska, A. (Med. Acad., Gdansk, Poland) and H. Kozłowski. Neoplasma (Bratisl.) 16(5): 549-556, 1969.

70-2669 CASE OF DEVELOPMENT OF CANCER FROM MARGINAL DIVERTICULUM OF THE ESOPHAGUS. (Rus.) Davydenko, V. A. (Acad. Milit. Med., Leningrad, USSR). Vestn. Rentgen. Radiol. 45(1): 89-90, 1970.

70-2670 CARCINOMA OCCURRING IN PHARYNGOESOPHAGEAL DIVERTICULUM: REPORT OF THREE CASES. (E.) Wychulis, A. R. (Mayo Clin., Rochester, Minn.), G. H. Gunnlaugsson and O. T. Clagett. Surgery 66(6):976-979, 1969.

70-2671 MALIGNANT DEGENERATION OF AN EPITHELIAL NEVUS. (E.) Swint, R. B. and S. N. Klaus (Yale U. Sch. Med., New Haven, Conn.). Arch. Derm. (Chicago) 101(1):56-58, 1970.

70-2672 CASE OF PEUTZ-JEGHERS SYNDROME WITH MALIGNANT DEGENERATION. (Ger.) Gasser, U. (Canton Hosp. Surg. Clin., Luzern, Switzerland) and A. Arquint. Schweiz. Med. Wschr. 99(52): 1894-1895, 1969.

See also abstract nos: 2151,2152,2153,2165,2456,2499,2558,2595,2605,2609

AUTHOR INDEX

- aronson, S. A. 2358
 belev, G. I. 2348
 bell, M. R. 2331
 dams, C. 2474
 dams, R. A. 2470
 derca, I. 2449
 dler, S. P. 2506
 dzhigitov, F. I. 2406,2410
 garwal, M. K. 2243
 garwal, S. 2531
 geenko, A. I. 2413
 huja, E. M. 2571
 leksandrowicz, J. 2135
 lford, T. C. 2405
 llcroft, R. 2294
 llen, A. 2319
 llen, J. R. 2308
 l-Saadi, A. A. 2629
 l'tshtein, A. D. 2413,2430,
 2433,2450
 ndersen, R. A. 2322
 nderson, D. E. 2456
 nderson, J. 2511
 nderson, T. J. 2281
 ngervall, L. 2545
 nkerst, J. 2401
 ntonov, A. M. 2304
 nki, T. 2351
 nchi, H. 2546
 nkhangel'skii, A. V. 2304
 nrmstrong, W. F. 2266
 naud, C. D. 2651
 nstein, P. 2392
 quint, A. 2672
 rhenius, E. 2240,2241
 ch, B. B. 2416
 nkenazi, A. 2431
 hley, D. J. B. 2558
 hanasiu, P. 2371
 erbach, H. 2124,2299
 tsyn, A. P. 2478
 elsson, U. 2471

 bakova, S. V. 2413
 cigalupo, G. 2228
 iley, P. C. 2643
 lduzzi, P. 2387,2464
 ldwin, R. W. 2271
 luda, M. A. 2377,2378
 rbanti-Brodano, G. 2441
 rry, E. J. 2242
 rtle, K. D. 2218
 silico, C. 2461,2465
 skar, J. F. 2390
 tes, R. R. 2223
 teson, E. M. 2533
 ther, R. 2648
 m, S. G. 2420
 ardsley, R. E. 2500
 ierwaltes, W. H. 2629
 litskii, G. A. 2202,2219

 Ben-Bassat, H. 2427
 Bendová, H. 2207
 Benemanskii, V. V. 2280
 Bengtsson, U. 2545
 Bennett, M. 2338
 Ben-Porath, M. 2175
 Bentvelzen, P. 2399
 Berg, J. W. 2556
 Berg, P. 2469
 Berge, T. 2583
 Berger, B. W. 2162
 Berman, L. D. 2423
 Bernard, J. 2594
 Berndt, H. 2587
 Bernelli-Zazzera, A. 2262
 Beskrovnyi, A. M. 2226
 Billheimer, F. E. 2439
 Bingham, E. 2301
 Biriulina, T. I. 2373
 Biserte, G. 2404
 Black, P. H. 2423,2424
 Blair, P. B. 2396,2398
 Bleiberg, M. J. 2323
 Bloch, M. 2175
 Blumberg, B. S. 2591
 Blumenshine, J. A. 2312
 Blumenson, L. E. 2613
 Bobrina, K. G. 2547
 Bock, F. G. 2205
 Bolande, R. P. 2656
 Bole, G. G. 2639
 Boone, C. W. 2645
 Borisiuk, Iu. P. 2215,2307
 Borsos, T. 2633
 Bosch, A. 2574
 Boulanger, P. A. 2404
 Boutibonnes, P. 2121,2296
 Bowen, J. 2456
 Bradshaw, E. 2542
 Brand, I. 2300
 Brand, K. G. 2300
 Brändli, O. 2526
 Braunwald, J. 2498
 Breslavskii, A. S. 2226
 Bresnick, E. 2325
 Bresson, M.-L. 2302
 Brière, N. 2258
 Brooke, B. N. 2655
 Brooks, R. E. 2332
 Broustet, A. 2151
 Brown, E. 2136
 Brown, M. 2434
 Brues, A. M. 2124,2299
 Bruevich, T. S. 2211
 Brunet, M. 2521
 Bulay, O. M. 2329
 Bundschuh, M. 2520
 Buoen, L. C. 2300
 Burbank, F. 2544
 Burdette, W. J. 2118
 Burdon, R. H. 2281
 Burke, J. G. 2412

 Burkitt, D. P. 2520
 Burmester, B. R. 2149
 Bushnell, D. E. 2256
 Bussey, H. J. R. 2654
 Butel, J. S. 2419,2421
 Byatt, P. 2632
 Bykovskii, A. F. 2459

 Cajone, F. 2262
 Calafat, J. 2399
 Calvert, J. 2286
 Cantor, C. R. 2245
 Cardiff, R. D. 2398
 Carey, J. J. H. 2590
 Carles-Trochain, E. 2152
 Carlton, W. W. 2649
 Carp, R. I. 2451
 Carstens, L. A. 2308
 Carter, A. P. 2528
 Carter, B. J. 2660
 Carter, R. L. 2315
 Cassidy, J. T. 2639
 Cattani, A. 2302
 Cellier, K. M. 2611
 Chai, C. K. 2644
 Chameaud, J. 2171
 Chan, S. P. 2370
 Chang, S. S. 2369
 Chapenko, S. V. 2365
 Chavez, R. F. 2229
 Chayen, J. 2271
 Chen, C. C. 2251
 Chen, K. P. 2567
 Cherepanova, A. I. 2216,2217
 Cherkasskii, L. A. 2231
 Chigirinskii, A. E. 2433
 Chirigos, M. A. 2370
 Choi, N. W. 2579,2580
 Christopherson, W. M. 2571
 Chumakov, M. P. 2440
 Ciufecu, E. 2371
 Clagett, O. T. 2670
 Clark, H. F. 2497
 Clarke, J. K. 2393
 Clayson, D. B. 2253
 Clayton, J. 2570
 Coghill, S. L. 2424
 Colby, C. 2386
 Colombies, P. 2152
 Cooke, E. M. 2178
 Cooke, R. A. 2532
 Cooper, P. 2570
 Cremer, N. E. 2356
 Crocker, T. T. 2287
 Crofton, E. C. 2536
 Croissant, O. 2473
 Cronin, M. T. I. 2249
 Crosswhite, L. 2635
 Cudkowicz, G. 2343
 Cuzin, F. 2469

- Daams, J. H. 2399
 Dahlin, K. 2520
 Dahlin, L. 2520
 Dausset, J. 2594
 Davidsohn, I. 2626
 Davies, J. N. P. 2562
 Davis, R. C. 2183
 Davis, R. H. 2268
 Davydenko, V. A. 2669
 Dawson, K. M. 2253
 Deaner, R. M. 2541
 Deardorff, W. L. 2482
 Declève, A. 2333, 2334
 Defendi, V. 2448
 Degos, L. 2594
 de Harven, E. 2351
 Deinhardt, F. 2504
 Dekegel, D. 2589
 del ande Eaton, S. 2223
 de Petris, S. 2362
 Dermott, E. 2393
 DeRoche, G. M. 2124, 2299
 Detroy, R. W. 2297
 deVaux Saint Cyr, C. 2507
 Deys, B. F. 2667
 Diad'kova, A. M. 2376, 2380
 Dieckmann, M. 2469
 Diengdoh, J. V. 2271
 Dikun, P. P. 2208, 2209, 2210
 Dimant, I. N. 2284
 Diring, H. 2221
 Dixon, C. B. 2423, 2424
 Dixon, J. A. 2552
 Dmochowski, L. 2364
 Doane, F. W. 2472
 Dodonova, N. N. 2413, 2430, 2433
 Doell, R. G. 2389
 Doi, T. 2488
 Doniach, I. 2174
 Dörken, H. 2606
 Dougan, L. 2625
 Dowling, A. M. 2455
 Downing, A. 2556
 Draganov, I. 2199
 Drechslerová, E. 2207
 Dreyfuss, Y. 2634
 Driscoll, D. H. 2612
 Dubbs, D. R. 2434, 2435, 2452
 Ducos, J. 2152
 Duff, R. 2422
 Duk, I. L. 2383
 Dunn, T. B. 2628
 Duryee, W. R. 2309
 Dutsić, S. 2549
 Dzagurov, S. G. 2382
- Eagle, H. 2470
 Echave Llanos, J. M. 2617
 Edlin, G. 2386
 Efimov, V. P. 2666
- Ehrenreich, T. 2634
 Elekoev, K. A. 2382
 Eligulashvili, R. K. 2365
 Emshanova, A. V. 2208, 2209
 Eneroth, C.-M. 2584
 Engel'gardt, N. B. 2348
 Enomoto, H. 2166
 Enterline, P. E. 2539, 2540
 Erb, P. 2407
 Erb, R. J. 2186
 Erokhin, R. A. 2176, 2177
 Esber, H. J. 2317
 Escalera, G. A. 2306
 Estampe, B. 2594
 Estes, J. D. 2392
 Evans, M. J. 2408
 Ezdinli, E. Z. 2635
- Fabian, F. 2497
 Fabiani, A. 2283
 Fabrikant, J. I. 2164, 2614
 Fahmy, M. J. 2289
 Fahmy, O. G. 2289
 Falk, H. L. 2301
 Fekety, F. R., Jr. 2590
 Fendell, L. D. 2313
 Ferrero, M. E. 2262
 Fields, C. 2136
 Filipiak, B. 2295
 Fink, L. M. 2250
 Fink, M. A. 2491
 Fischinger, P. J. 2359
 Fisher, J. C. 2183
 Flaks, A. 2188
 Fleissner, E. 2374
 Fletcher, R. 2220
 Fogh, H. 2455
 Fogh, J. 2453, 2454, 2455, 2509, 2510
 Foley, G. E. 2470
 Franklin, R. 2555
 Fraumani, J. F., Jr. 2518, 2544
 Frías, Z. 2574
 Friedman, M. P. 2400
 Friend, C. 2343
 Frisch, W. 2153
 Frohworth, N. 2221
 Frolov, A. F. 2291
 Froman, C. 2581
 Fry, R. J. M. 2178, 2247, 2248
 Fujii, K. 2264
 Fujinaga, S. 2364
 Fujtia, H. 2409
 Fullmer, C. D. 2319
 Fulton, R. E. 2472
 Furer, N. M. 2346
 Fuse, Y. 2154
 Fushimi, K. 2314
- Gadomska, H. 2524
 Gaffney, E. V. 2453, 2455, 2509
 Gaja, G. 2262
 Gamburg, V. P. 2429
 Gandagule, V. N. 2531
 Garbe, E. 2521
 Garcia, J. S. 2593
 Gardner, L. I. 2316
 Gardner, M. B. 2392
 Gardner, M. J. 2537
 Gasser, U. 2672
 Gay, F. W. 2393
 Gazdar, A. F. 2367
 Geering, G. 2489
 Georgescu, D. C. 2515
 Gerber, P. 2143, 2480, 2482
 Gerstley, B. J. S. 2591
 Gertman, P. M. 2279
 Ghosh, I. 2630
 Ghosh, S. 2630
 Gibson, R. 2592
 Gilden, R. V. 2335, 2360, 2369, 2390, 2588
 Gilgen, A. 2214
 Gilmour, J. 2557
 Ginsberg, H. S. 2400
 Giovannella, B. C. 2157
 Gitter, S. 2267
 Glass, R. M. 2249
 Gnosspeilus, Y. 2204
 Goldberg, M. 2265
 Goldé, A. 2381
 Goldenberg, D. M. 2664
 Goldman, M. 2255
 Goloviznin, G. I. 2376
 Gorelova, N. D. 2216, 2217
 Görlich, M. 2228
 Gorodilova, V. V. 2413
 Graham, J. B. 2568
 Graham, S. 2592
 Grahn, D. 2178
 Gray, C. 2497
 Green, H. 2461
 Green, M. 2145
 Gretskaia, O. P. 2208, 2209
 Griesbach, L. M. 2185
 Griffin, A. C. 2255
 Grogan, D. E. 2285
 Groot, E. H. 2278
 Gross, J. 2175
 Gross, K. 2646
 Gross, L. 2634
 Gross, S. 2564
 Grossi-Paoletti, E. 2283
 Groupé, V. 2379
 Grube, D. D. 2124, 2299
 Grunberger, D. 2245
 Gubeladze, D. A. 2406
 Guentzel, M. J. 2419
 Guest, B. A. 2576
 Guir, J. 2498
 Guillen, W. H. 2579, 2580
 Gunnlaugsson, G. H. 2670

Gurda, M. 2595
Gurtsevich, V. E. 2354
Gutmann, H. R. 2242,2251

Hackett, A. J. 2398
Hafeez, M. A. 2573
Haga, M. 2314
Hahn, E. C. 2446,2454
Hahn, G. M. 2333,2334
Haidak, G. L. 2159
Hamazaki, Y. 2318
Hamburg, V. P. 2418
Hämmerling, U. 2351
Hampar, B. 2480
Hanafusa, H. 2385
Hanafusa, T. 2385
Hanaki, A. 2260
Hancock, R. 2144
Hanna, M. G., Jr. 2349
Hare, J. D. 2458,2464
Harrington, J. S. 2122
Harris, A. W. 2640
Hartley, J. W. 2353
Hartley, M. W. 2643
Harvey, J. J. 2362
Hatanaka, M. 2360,2369
Hayashi, K. 2665
Hayashi, M. 2260
Hayat, M. 2302
Häyry, P. 2448
Heath, C. W., Jr. 2593
Hecker, W. 2443,2444,
2445
Heidelberger, C. 2123,2155,
2185,2221
Heise, E. 2228
Hempelmann, L. H. 2173
Henle, G. 2481
Henle, W. 2481
Henry, P. H. 2424
Herberman, R. B. 2457,2505
Herman, B. 2540
Hesseltine, C. W. 2297
Hewetson, J. F. 2379
Heyl, T. 2527
Hiasa, Y. 2235
Hicks, R. M. 2254
Higginson, J. 2561
Hill, B. J. 2651
Hill, H. C. 2266
Hillström, L. 2529
Hinze, H. C. 2475
Hirayama, T. 2596,2599
Hirono, I. 2314
Hitosugi, M. 2538
Hoffman, N. R. 2551
Hoffmann, D. C. 2655
Hoffmann, H. D. 2206
Hollinshead, A. 2405
Holzmann, H. 2153
Hook, R. H. 2312
Hook, W. A. 2370
Horibata, K. 2640
Horowitz, I. 2539

Hosokawa, M. 2341
Hsu, K. C. 2480
Huang, C. C. 2262,2631,
2663
Huebner, R. J. 2353,2369,
2390,2392,2405,2588
Hulu, N. 2610
Hummeler, K. 2442,2508
Humphrey, R. R. 2650

Iakovleva, L. A. 2503
Ichimaru, M. 2603
Ievleva, E. S. 2348
Iftimovici, M. 2449
Imamura, T. 2631,2663
Inbar, M. 2427
Inoue, Y. K. 2402,2403
Irino, H. 2190,2665
Irlin, I. S. 2459
Isaacs, J. J. 2490
Israilian, A. A. 2284
Ito, Y. 2187
Iuzvinkevich, A. K. 2657
Ivanova, O. Iu. 2202
Iwa, N. 2488
Iype, P. T. 2185

Jackson, J. L. 2628
Jacquet, J. 2121,2296
Jainchill, J. L. 2358,2436
Jameson, M. H. 2572
Janicki, J. 2295
Janss, D. H. 2327
Jellinck, P. H. 2220
Jensen, F. C. 2508
Jernstrom, P. 2632
Johansson, S. 2545
Johnson, J. 2160
Johnson, K. H. 2300
Jones, D. W. 2218
Jones, E. W. 2527
Jones, J. C. 2312
Jones, R. F. 2416
Jordan, R. 2622
Josey, W. E. 2576
Jung, E. G. 2311
Just Viera, J. O. 2306

Kalinina, I. A. 2210
Kalman, E. 2200
Kalnins, Z. A. 2660
Kalomiris, C. G. 2612
Kamei, Y. 2605
Kamibayashi, K. 2597
Kampschmidt, R. F. 2652
Kang, H. S. 2439
Kantor, I. 2162
Kaplan, E. L. 2651
Kaplan, H. S. 2333,2334
Karewicz, Z. 2524
Kariyone, S. 2167
Karsch, P. 2664

Karzon, D. T. 2497
Kasper, T. A. 2570
Kastelan, A. 2196
Katayama, H. 2172
Kato, H. 2559
Kato, S. 2488
Kauffman, C. 2331
Kawakami, H. 2170
Kawarai, M. 2189
Kay, H. E. M. 2641
Keith, L. 2136
Keller, A. Z. 2530
Keller, G. H. M. 2278
Kern, J. 2588
Kessler, I. I. 2519,2586
Kesterson, J. W. 2649
Ketcham, A. S. 2658
Keybets, M. J. H. 2278
Khan, M. H. 2637
Khazov, P. D. 2158
Khesina, A. Ia. 2202,2211,
2219
Khristov, K. 2257
Kimura, I. 2187
Kimura, T. 2403
King, G. S. 2491
King, S. 2316
Kirkland, J. A. 2611
Kirkwood, J. M. 2489
Kirn, A. 2498
Kisule, A. 2609
Kit, S. 2434,2435,2452
Kitabatake, T. 2168,2604
Klauber, E. 2259
Klaus, S. N. 2671
Klein, M. 2249
Kleinschmidt, A. K. 2465
Kneale, G. W. 2169
Knospe, W. H. 2636
Ko, R.-T. 2567
Kobayashi, H. 2341,2344,
2345,2597
Kobayashi, J. 2264
Kodama, M. 2203
Kodama, T. 2341,2344
Kodama, Y. 2205
Kogan, A. Kh. 2117
Kolesnichenko, T. S. 2290
Kołodziejska, H. 2524
Kondrikov, N. I. 2661
Koprowski, H. 2441,2470
Kornitskii, M. A. 2231
Korosteleva, T. A. 2234
Korsak, E. 2638
Koshurnikova, N. A. 2176,
2177
Koszarowski, T. 2524
Kovacs, K. 2227
Kozlowski, H. 2668
Krajinović, S. 2549
Král, V. 2207
Kramarsky, B. 2399
Krasnitskaia, N. D. 2208,
2209
Kriek, E. 2244

- Krivoshapkin, V. G. 2548
 Krivoshein, Iu. S. 2406,2410
 Krylova, N. V. 2117
 Kryukova, I. N. 2372
 Kukain, R. A. 2365
 Kupchinskii, L. G. 2375
 Kurakane, K. 2554
 Kurihara, N. 2601
 Kurihara, T. 2198
 Kurimura, T. 2434,2452
 Kurita, S. 2605
 Kurohara, S. S. 2568
 Kurokawa, S. 2168,2604
 Kutsukata, A. 2170
 Kuznetsov, O. K. 2376,2380
 Kuznetsova, N. N. 2373
- Lafuma, J. 2171
 Lambert, P. M. 2535
 Lampert, F. 2664
 Lampert, P. W. 2496
 Lane, M. 2285,2286
 Lanzi, R. L. 2331
 Lapin, B. A. 2503
 Lapshin, I. I. 2208
 Laron, Z. 2267
 Lasfargues, E. Y. 2399
 Lavrova, N. A. 2202
 Lawler, S. D. 2641
 Lawson, T. A. 2253
 Lazarus, H. 2470
 Lea, A. J. 2133
 Leach, W. B. 2643
 Leaf, D. S. 2251
 Leahy, M. S. 2266
 Leavesley, G. M. 2625
 Lee, D. J. 2330
 Lee, J. A. H. 2528
 Lee, Y. K. 2588
 Leibman, K. C. 2310
 Leff, J. 2500
 Legrand, E. 2151
 Lemberg, V. K. 2176,2177
 Leńczyk, M. 2550
 Lennert, K. 2607
 Lennette, E. H. 2588
 Lesko, S. A., Jr. 2206
 Levenbuk, I. S. 2433
 Levij, I. S. 2230
 Levin, M. 2592
 Levin, M. J. 2424
 Levine, A. J. 2437,2439, 2447
 Levine, E. M. 2470
 Levine, W. G. 2324
 Levisohn, R. 2252
 Levy, L. S. 2315
 Lewis, A. M., Jr. 2425,2426
 Liebelt, A. 2286
 Liebelt, R. A. 2285,2286
 Lieberman, M. 2333,2334
 Lief, F. S. 2508
 Lilienfeld, A. 2592
 Lilly, F. 2336
- Lin, T.-M. 2565,2567
 Lindberg, U. 2467
 Lindsay, S. 2132
 Links, J. 2394
 Lipova, V. A. 2209
 Lipschitz, R. 2581
 Litvinov, N. N. 2280
 Lombart, A., Jr. 2259
 Lockhart-Mummery, H. E. 2654
 Löffler, H. 2443
 Loh, P. M. 2308
 Loktionov, G. M. 2284
 Lombardi, P. S. 2464
 London, W. T. 2591
 Loveless, J. 2453,2455
 Lowe, C. R. 2565
 Luce, C. F. 2576
 Lukes, R. J. 2556
 Lumb, J. R. 2389
 Lundin, F. E., Jr. 2571
 Lunger, P. D. 2495
 Lungu, M. 2371
 Lunts, A. M. 2304
 Lyons, M. J. 2400
- MacMahon, B. 2565,2566
 Macpherson, L. W. 2472
 MacVaugh, H., III 2160
 Madden, J. W. 2279
 Maeda, K. 2166
 Mafigiri, J. 2609
 Maher, V. M. 2239
 Malejka-Giganti, D. 2242
 Malendowicz, L. 2295
 Manaker, R. A. 2138
 Mandavia, M. 2265
 Manelis, M. E. 2575
 Maňka, I. 2259
 Mannering, G. J. 2326
 Mannick, J. A. 2183
 Manning, J. S. 2398
 Mariage, C. 2292,2293
 Marmol, F. R. 2477
 Martin, H. 2637
 Martos, L. M. 2480
 Martynova, R. P. 2282
 Massé, H. 2522
 Masse, R. 2171
 Matovinovic, J. M. 2266
 Matsukura, M. 2340
 Matsushima, T. 2246
 Matsuya, Y. 2461
 Matsuzaki, M. 2260
 Matthews, R. S. 2218
 Mazurenko, N. P. 2354
 McCollister, S. B. 2312
 McCormick, K. J. 2511
 McDonald, R. 2504
 McGowan, L. 2268
 McInerney, R. P. 2159
 McKinnell, R. G. 2494
 McLaughlin, B. C. 2411
 McPhedran, P. 2593
- McSwain, B. 2555
 Mega, T. 2546
 Mekler, L. B. 2384
 Mel, H. C. 2398
 Melnick, J. L. 2588
 Mendez, W. M. 2571
 Merekalova, Z. I. 2342
 Merkow, L. P. 2414,2417
 Meuge, C. 2151
 Meyer, G. 2466
 Meyer, J. A. 2615
 Mietkiewski, K. 2295
 Milcu, S. M. 2181
 Millard, R. E. 2641
 Miller, E. 2368
 Miller, E. C. 2238,2239
 Miller, J. A. 2238,2239
 Miller, R. W. 2137,2518
 Millman, I. 2591
 Minakami, T. 2264
 Minowada, J. 2631
 Mirand, A. G. 2352
 Mirand, E. A. 2352
 Mirra, A. P. 2565
 Mirvish, S. S. 2221
 Mita, T. 2275
 Mitchell, R. E. 2161
 Mitiushin, V. M. 2375
 Miura, M. 2191
 Miura, T. 2277
 Miyake, S. 2462
 Miyake, T. 2187
 Miyamoto, T. 2385
 Miyata, H. 2166,2597
 Mizell, M. 2489,2490,2491
 Mizutani, S. 2388
 Mohr, U. 2237
 Mokuno, J. 2600
 Mondal, S. 2185
 Money, W. L. 2119
 Monjour, L. 2292,2293
 Montgomery, P. O., Jr. 2276
 Moon, R. C. 2327
 Moore, G. E. 2262,2631, 2663
 Moore, L. A. 2634
 Mora, P. T. 2432
 Mordkovich, M. S. 2215
 Morehead, R. P. 2660
 Morgan, D. L. 2223
 Morgen, H. R. 2387,2464
 Morganroth, J. 2432
 Mori, M. 2154
 Morinaga, K. 2554
 Moriyama, Y. 2274
 Morozov, K. V. 2382
 Morrow, R. H. 2609
 Morton, J. I. 2332,2347
 Moslander, V. 2552
 Mouriquand, C. 2397
 Mouriquand, J. 2397
 Mukerjee, D. 2456
 Muller, M. 2585
 Mulligan, T. O. 2523
 Munakata, H. 2275

- Murao, T. 2318
 Murayama, F. 2499
 Murphy, W. H. 2331
- Nadler, N. J. 2265
 Nagaeva, L. I. 2365
 Nagaharu, T. 2264
 Nagashima, T. 2170
 Nagata, C. 2203
 Nahmias, A. J. 2576
 Naib, Z. M. 2576
 Nakahara, W. 2275
 Nakajima, Y. 2264
 Nakamura, Y. 2402
 Nash, R. E. 2617
 Nastac, E. 2371
 Nathans, D. 2506
 Nayak, D. P. 2377,2378
 Nazerian, K. 2149,2485,
 2486,2487
 Neale, R. 2520
 Neaves, A. 2612
 Nelson, J. H. 2245
 Neu, R. L. 2316
 Neurath, G. 2156
 Newell, G. R. 2139
 Ng, A. B. P. 2621
 Ni, L. Y. 2626
 Nicoli, J. 2466
 Nielson, B. 2287
 Niezabitowski, A. 2357
 Nifatov, A. P. 2176,2177
 Nishibe, Y. 2402,2403
 Nishimura, M. 2321
 Nishimura, S. 2250
 Nishio, T. 2264
 Nishiyama, H. 2600
 Nolan, J. F. 2632
 Norback, D. H. 2308
 Nordenskjöld, B. A. 2467
 Nosek, H. 2550
- Obukh, I. B. 2372
 O'Connor, T. E. 2359
 O'Connor, G. T. 2148
 Odaka, T. 2240,2339
 Oehlert, W. 2127
 Ogloblina, I. A. 2211
 Okada, Y. 2499
 Okano, T. 2277
 Okita, T. 2598,2602
 Old, L. J. 2351,2489
 Olsen, R. G. 2477
 Ono, K. 2488
 Onoé, T. 2154
 Orszlan, S. 2335
 Orrenius, S. 2204
 Orth, G. 2473
 Oshiro, L. S. 2356
 Oszacki, J. 2550
 Ota, K. 2600
 Otten, J. 2589
 Oxford, J. S. 2411,2415
- Padgett, B. L. 2476
 Paoletti, P. 2283
 Pardo, M. 2414,2417
 Parker, J. E. 2571
 Parkinson, A. T. 2159
 Parks, T. G. 2654
 Patterson, D. S. P. 2294
 Paul, J. S. 2276
 Pauluzzi, S. 2421
 Peacock, E. E., Jr. 2279
 Pearson, G. 2481
 Peraino, C. 2247,2248
 Perraud, R. 2171
 Peskin, G. W. 2651
 Peydro, A. 2259
 Pierce, W. S. 2160
 Pike, M. C. 2609
 Pilch, Y. H. 2658
 Pliss, G. B. 2272
 Pliss, M. B. 2261
 Podell, R. N. 2563
 Poel, W. E. 2364
 Pogosiants, E. E. 2642,
 Polliack, A. 2230
 Popovskii, V. G. 2215
 Potapenkova, L. S. 2234
 Potter, C. W. 2411,2415
 Potter, V. R. 2256
 Powers, H. O. 2316
 Powell, R. D., Jr. 2658
 Prandetskii, A. P. 2657
 Pretlow, T. G., II 2645
 Prigozhina, E. L. 2202,2642
 Probatova, N. A. 2354
 Proshchenko, V. G. 2395
 Purchase, H. G. 2149,2483,
 2484,2485
 Purchase, I. F. H. 2298
 Puzyrev, A. A. 2176,2177
 Pylev, L. N. 2201
 Pyieva, Z. A. 2182,2195
- Ramming, K. P. 2658
 Ramos, L. 2455
 Ramot, B. 2610
 Randall, C. L. 2577
 Rangelova, S. 2142
 Rapoza, N. P. 2414,2417
 Rapp, H. J. 2588,2633
 Rapp, F. 2419,2421,2422,
 2438,2588
 Raska, K., Jr. 2512
 Rauscher, F. J., Jr. 2146
 Rausing, A. 2471
 Ravisse, P. 2514
 Ravnihar, B. 2565
 Rawls, W. E. 2474
 Rawson, R. W. 2119
 Reagan, J. W. 2621
 Redmond, D. E., Jr. 2115
 Reid, D. D. 2535
 Reiskin, A. B. 2125,2126
 Renwick, D. H. G. 2569
 Reyes, E. L. 2553
- Rhyne, A. L. 2660
 Richards, W. P. C. 2391
 Richey, D. J. 2150
 Rickard, C. G. 2392
 Riddle, M. 2647
 Riggs, J. L. 2588
 Ritzi, E. 2437
 Robertson, J. D. 2559
 Roe, F. J. C. 2201,2315
 Roehm, J. N. 2330
 Roizman, B. 2147
 Romanov, K. P. 2376
 Römer, K.-H. 2543
 Rongey, R. W. 2392
 Ronichevskaia, G. M. 2282
 Rosenkrantz, H. 2317
 Rosin, A. 2175
 Rossi, G. B. 2343
 Rowe, W. P. 2353,2420,2425,
 2426
 Rubenchik, B. L. 2261,2263
 Ruchkovskii, B. S. 2215,2307
 Ruffié, J. 2152
 Ruiter, M. 2501
 Russell, W. J. 2172
 Rust, J. M. 2178
 Rwomushana, J. W. 2230
 Ryan, J. P. 2268
 Rydell, R. E. 2251
- Sabashvili, M. K. 2346
 Sacher, G. A. 2178
 Sachs, L. 2427
 Sadek, S. E. 2312
 Saito, H. 2341,2344
 Sakai, K. 2260
 Sakharov, I. I. 2666
 Sakurai, M. 2560
 Salber, E. J. 2565
 Sallese, A. R. 2125,2126
 Samoilina, N. L. 2202
 Samokhodskii, V. N. 2534
 Sandberg, A. A. 2635
 Sanford, K. K. 2628
 Sanguliia, B. A. 2406
 Sano, T. 2320
 Sapatino, V. 2449
 Sarma, P. S. 2390,2392
 Sarycheva, O. F. 2430,2433,
 2450
 Sasaoka, I. 2665
 Sassy, C. 2466
 Sataev, M. M. 2284
 Sauer, G. 2446
 Savost'ianov, G. A. 2380
 Sawada, S. 2172
 Sawayama, K. 2502
 Schaad, R. 2214
 Schauer, A. 2273
 Scherbakova, O. E. 2418
 Schiffer, D. 2283
 Schild, G. C. 2415
 Schochet, S. S., Jr. 2496

- Schonland, M. 2542
 Schreiber, W. M. 2559
 Schrek, R. 2636
 Schriba, M. 2481
 Schulte-Holthausen, H. 2479
 Schuman, L. 2592
 Schuman, L. M. 2579,2580
 Scribner, J. D. 2238
 Segi, M. 2601
 Sekirov, B. A. 2282
 Selim, M. A. 2568
 Sendo, F. 2341,2345
 Sera, Y. 2321
 Sergeev, A. V. 2350
 Shabad, L. M. 2116,2128, 2202
 Shakhlov, V. A. 2478
 Shapiro, M. J. 2163
 Shapiro, S. 2564
 Shcherbak, N. P. 2213
 Shcherbakova, O. E. 2429
 Sheehan, W. 2610
 Shein, H. M. 2460
 Shendrikova, I. A. 2208,2209
 Shevliagin, V. Ia. 2373,2375, 2384
 Shibuya, C. 2303,2314,2665
 Shima, H. 2264
 Shirai, K. 2236
 Shirai, T. 2341
 Shliankevich, M. A. 2384
 Shoeman, D. W. 2326
 Short, J. G. 2319
 Shuklinov, V. A. 2222
 Siegel, B. V. 2332,2347
 Siegler, R. 2363
 Sigüenza, R. F. 2480
 Silich, A. A. 2215
 Simons, P. J. 2361
 Sinnhuber, R. O. 2330
 Sjögren, H. O. 2401
 Skoog, L. 2467
 Slifkin, M. 2414,2417
 Smart, C. R. 2552
 Smirnov, G. A. 2212
 Smirnova, N. E. 2382
 Smith, B. J. 2463
 Smith, C. J. 2225
 Smith, C. K. 2639
 Smith, E. S. O. 2570
 Smith, F. E. 2285
 Smith, G. 2220
 Smith, J. B. 2134
 Smith, J. R. 2313
 Smith, R. W. 2432
 Smolen, V. F. 2186
 Sneider, T. W. 2256
 Snyder, D. E. 2186
 Snyder, S. 2504
 Snyder, S. P. 2391
 Sokal, J. E. 2635
 Sokol, F. 2442,2451
 Sokova, O. I. 2642
 Soloimskaia, E. A. 2232
 Somogyi, A. 2227
 Sorokina, Iu. D. 2224
 Soszka, S. 2624
 Sowers, J. A. 2322
 Spärck, J. V. 2627,2646
 Speiser, V. 2267
 Spencer, H. C. 2312
 Sprague, R. 2317
 Sprecher-Goldberger, S. 2589
 Stackpole, C. W. 2490,2492
 Staffeldt, E. 2178,2248
 Stanley, M. A. 2611
 Stanton, M. F. 2368
 Staszewski, J. 2524, 2525
 Statnikov, A. M. 2547
 Stavrou, D. 2269,2270
 Stavrovskaja, A. A. 2202
 Steeves, R. A. 2338
 Stepanova, G. N. 2354
 Stewart, A. M. 2169
 Stim, T. B. 2337
 Stoian, M. 2371
 Strax, P. 2564
 Strohl, W. A. 2512
 Stromskaia, T. P. 2288
 Stück, B. 2351
 Suhrbier, K. 2616
 Suit, H. D. 2196
 Sukacheva, O. A. 2226
 Šula, J. 2207
 Summers, W. C. 2239
 Sunderman, F. W., Jr. 2310
 Sutnick, A. I. 2591
 Sutton, H. 2616
 Suzuki, S. 2179
 Svet-Moldavsky, G. J. 2418
 Swanbeck, G. 2529
 Swetly, P. 2441
 Swint, R. B. 2671
 Sykes, J. A. 2632
 Szakal, A. K. 2349
 Szepsenwol, J. 2328
 Szwagrzyk, E. 2582
 Szydłowska, H. 2582
 Takahashi, M. 2631
 Takeda, K. 2141
 Takeichi, T. 2341
 Talash, M. 2440
 Talerman, A. 2608
 Talley, R. W. 2553
 Tam, M. R. 2331
 Tandon, P. L. 2573
 Tarin, D. 2184
 Taşcă, C. V. 2516
 Tasseron, J. G. 2221
 Taylor, D. O. N. 2356
 Teeter, A. 2287
 Teitz, Y. 2356
 Temin, H. M. 2388
 Teppo, L. 2578
 Teresky, A. K. 2447
 Tevethia, S. S. 2428
 Theilen, G. 2504
 Theilen, G. H. 2391
 Thiry, L. 2589
 Thor, H. 2204
 Tiktin, L. A. 2215,2307
 Ting, C.-C. 2457
 Ting, R. C. 2368
 Todaro, G. J. 2358,2436
 Todd, D. 2570
 Tol, O. 2394
 Tomassini, N. 2442
 Tomii, S. 2546
 Tompkins, W. A. F. 2474,2475
 Toni, R. J. 2369,2390
 Torealm, N. G. 2583
 Torpier, G. 2404
 Tot, F. 2372
 Toto, P. D. 2229
 Towler, W. F. 2656
 Trachsel, B. 2311
 Trentin, J. J. 2412,2511
 Trichopoulos, D. 2565
 Trobaugh, F. E., Jr. 2636
 Trubcheninova, L. P. 2383,2429
 Trulock, S. C. 2438
 Trummer, M. J. 2541
 Tsetlin, E. M. 2413,2433
 Ts'o, P. O. P. 2206
 Turkington, R. W. 2647
 Turner, H. C. 2588
 Turner, W. 2370
 Tuyns, A. J. 2514
 Tweedell, K. S. 2493
 Tyndall, R. L. 2349
 Uchino, H. 2165
 Uekama, K. 2277
 Upchurch, H. F. 2652
 Urbanowicz, M. 2295
 Valaoras, V. G. 2565
 Van Der Watt, J. J. 2298
 Vane, F. 2326
 Van Hoosier, G. L., Jr. 2412
 van Mullem, P. J. 2501
 Vasil'ev, Iu. M. 2202
 Vasil'eva, N. N. 2305
 Vasquez, C. 2465
 Venet, L. 2564
 Venet, W. 2564
 Vernon, L. 2390
 Veskova, T. K. 2383
 Viala, C. 2397
 Vogler, W. R. 2482
 Vogt, M. 2468,2469
 Volkov, G. I. 2666
 Völlnagel, T. 2273
 von Kreybig, T. 2129
 von Metzler, A. 2192,2193,2194
 Voronin, E. S. 2382
 Vorvik, D. 2201

- Wahlqvist, L. 2545
Wakisaka, G. 2167
Wales, J. H. 2330
Walker, D. L. 2475,2476
Walker, J. L. 2480
Walker, K. 2319
Wallace, J. 2489
Wallace, J. D. 2612
Waller, R. E. 2537
Walrond, E. R. 2622
Warda, B. 2524,2623
Warren, S. 2131
Watanabe, K. 2180
Wattenberg, L. W. 2329
Waubke, R. 2481
Webb, S. J. 2648
Weil, C. S. 2130
Weil, R. 2144
Weinstein, I. B. 2243,2245,
2250
Weisburger, E. K. 2249
Weisburger, J. H. 2246,
2249
Wells, G. A. 2480
Wepsic, H. P. 2633
Wever, G. H. 2435
Whang-Peng, J. 2633
Whitescarver, J. 2632
Wieczorkiewicz, A. 2524,2525
Wiese, W. H. 2420,2426
Wildanger, F. 2273
Wilentz, J. M. 2162
Wilson, H. 2653
Wisniewski, L. 2638
Witter, R. L. 2149,2486
Wolfe, L. 2504
Wolff, G. L. 2618,2619,
2620
Woodard, G. 2249
Woodliff, H. J. 2625
Woods, D. A. 2225
World Health Organization
2513,2517
Wychulis, A. R. 2670
Yamane, Y. 2260
Yamasaki, M. 2168
Yamazaki, N. 2170
Yankee, R. A. 2591
Yeager, G. H. 2306
Yohn, D. S. 2408, 2416,2477
Yokoro, K. 2355
Yoshida, M. 2277
Yoshida, T. 2546
Yoshikura, H. 2366
Yoshinaga, H. 2172
Yost, Y. 2251
Yuasa, S. 2565,2566
Yuda, K. 2170
Yuspa, S. H. 2223
Zabezhinskii, M. A. 2233,2272
Zackheim, H. S. 2197
Zadik, Z. 2431
Zajac, B. A. 2481
Zavodova, T. I. 2440
Zbar, B. 2588,2633
Zeigel, R. 2497
Zharova, E. I. 2354
Zhavoronkov, A. A. 2478
Zheleznov, B. I. 2661
Zhuravleva, T. B. 2120
Zimmerman, J. 2512
Zolotareva, T. M. 2304
Zóltowska, A. 2668
zur Hausen, H. 2479

SUBJECT INDEX

- ABNORMALITIES, CONGENITAL
association with malignant tumors, children,
review: 2137
- ABNORMALITIES, DRUG-INDUCED (See Teratogenesis)
- ABSORPTION, INTESTINAL
dimethylbenzanthracene, rat: 2327
- ACETAMIDE, N-ACETOXY-N-ARYL-ESTERS
nucleophilic substitution, decomposition
pathways: 2238
- ACETAMIDE, THIO-
liver tumors, glycolysis and regulating enzymes,
rat: 2263
- ACETONE
production, intermediate pyrolytic resins,
skin tumors and leukemia, animal: 2304
- 2-ACETYLAMINOFLUORENE (See N-2-Fluorenylacetamide)
- ACTINOMYCIN D (See under Antitumor agents)
- ADHESIVES, SURGICAL
s.c. tumors, strain differences, mouse: 2306
- ADJUVANTS
Freund's, effect on transplantability of
adenovirus 12-induced hamster tumor: 2405
- ADRENAL MEDULLA
calcitonin-like factor, possible pathogenetic
significance, multiple endocrine tumor
syndrome (Type 2): 2651
- AFLATOXICOL
isolation (aflatoxin B1-treated steroid-hydrox-
ylating fungus) and structure: 2297
- AFLATOXIN(S)
analysis, foods and animal feeds of tropical
(African) or temperate (French) origin: 2296
effect on microorganisms, review: 2121
environmental, leukemia, Europe, review: 2135
induction of serum neoantigen, rat: 2293
liver tumors
pathology, rat: 2295
promotion, cyclopropanoid fatty acids, trout:
2330
serum esterases, rat: 2292
toxicity, liver, monkey: 2298
- AFLATOXIN B-1
metabolism, mammals and birds: 2294
transformation product from steroid-hydrox-
ylating fungus, structure: 2297
- AGE FACTORS
CNS disease induced by transplantable leukemia,
mouse: 2331
hydroxyfluorenylacetamide tumors, rat: 2249
leukemia epidemiology, aged, Georgia (Atlanta),
ethnic groups: 2593
malignant melanoma incidence, U.S.: 2528
methylcholanthrene tumors of lung transplants,
mouse: 2187
- Agrobacterium tumefaciens
bacteriophage PS-8, plant tumors: 2500
- AIR POLLUTION
benzpyrene
dust, Switzerland, urban (Zurich) and rural:
2214
review: 2116
bronchitis, Great Britain: 2535, 2536
fuel consumption, cancer epidemiology, France:
2521
- AIR POLLUTION, (Contd.)
lung cancer
Japan (Amagasaki and Nishinomiya): 2538
Scotland, urban and rural: 2536
smoking, East Germany: 2543
respiratory diseases, data evaluation methods:
2537
- ALCOHOL CONSUMPTION
brain tumors, Minnesota: 2580
esophagus cancer, Jamaica and Western
Australia, comparison: 2533
liver cirrhosis and hepatoma, Japan: 2560
- ALUMINUM-DEXTRAN
effect on methylcholanthrene tumors, rat: 2192
- AMIDES, AROMATIC
N-hydroxy-, esters, mutagenesis, bacteria:
2239
- AMINES, AROMATIC
DNA photosensitization: 2203
- AMINOPTERIN (See under Antitumor agents)
- ANEMIA, PERNICIOUS
stomach cancer, Minnesota (Minneapolis): 2551
- ANILINE, DIMETHYL-
effect on liver microsomes, rat: 2240, 2241
- ANTICOAGULANTS
effect on transplanted tumors, mouse: 2302
- ANTILYMPHOCYTE SERUM (See Immune serum)
- ANTITUMOR AGENTS (See also 6-Mercaptopurine)
actinomycin D
effect on methylcholanthrene skin tumors,
mouse: 2182
aminopterin
effect on liver or spleen tetrahydrofolate
dehydrogenase, mouse viral leukemias:
2350
bromodeoxyuridine
effect on
Marek's disease virus, chick or duck
embryo cells: 2487
Rous virus transformation, chick embryo
cells: 2387
busulfan or ³²P
effect on chromosomes, polycythemia vera:
2641
cyclophosphamide
effect on dimethylbenzanthracene cheek
pouch tumors, hamster: 2230
cytosine arabinoside
effect on Yaba poxvirus-infected cells:
2477
methotrexate
effect on dimethylbenzanthracene cheek
pouch tumors, hamster: 2230
prodigiosan (interferon-stimulating antibiotic)
effect on Friend virus leukemogenesis,
mouse: 2346
relationship of teratogenic and carcinogenic
activity, animal, review: 2129
vinblastine
effect on dimethylbenzanthracene cheek
pouch tumors, hamster: 2230
- ANUS NEOPLASMS
epidemiology
Jamaica: 2557

- NUS NEOPLASMS, (Contd.)
 epidemiology, (Contd.)
 Tennessee (Nashville), ethnic groups: 2555
 PNEUMECTOMY (See under Surgery)
 RSENIC
 mechanism of action, normal human cells: 2311
 SBESTOS
 benzpyrene-adsorbed, effect on benzpyrene
 uptake by lung, hamster: 2201
 occupational exposure, lung cancer, Japan:
 23.0, 2321
 TOBENZENE, 4-DIMETHYLAMINO-
 effect on liver enzymes, rat: 2260, 2261,
 2262, 2263
 liver tumors (rat): 2258, 2259, 2261, 2262,
 2263, 2264
 review: 2154
 TOBENZENE, 3'-METHYL-4-DIMETHYLAMINO-
 effect on RNA or DNA, rat liver: 2255, 2256
 review: 2154
 liver tumors (rat)
 effect of stress: 2179, 2180
 OTOLUENE, o-AMINO-
 effect on liver and serum proteins, mouse: 2234

 CTERIA
 effect of aflatoxins, review: 2121
 CTERIOPHAGE
 Agrobacterium tumefaciens, plant tumors: 2500
 INZANTHRACENE, 1,2:3,4-DI-
 effect on proteins, mouse skin: 2221
 INZANTHRACENE, 1,2:5,6-DI-
 mechanism of action, review: 2155
 specific carcinogen-binding skin protein,
 analysis, mouse: 2221
 IZ(a,h)ANTHRACENE, DI-
 metabolism, mouse embryo cells: 2219
 IZANTHRACENE, 7,12-DIMETHYL-
 absorption, rat: 2327
 carcinogenic effect, hamster strain (Phodopus
 sungorus): 2642
 cheek pouch tumors
 antibody staining patterns, hamster: 2229
 effect of antitumor agents, hamster: 2230
 ultrastructure of premalignant lesions,
 hamster: 2225
 DNA binding, mechanism, normal cells: 2223
 effect on differentiation, rat muscle cultures:
 2222
 mammary tumors (rat): 2226
 biochemical parameters of growth and
 regression: 2228
 effect of spironolactone: 2227
 metabolism
 effect of methylcholanthrene, rat liver
 microsomes: 2220
 mammalian fibroblasts, species differences:
 2202
 mouse embryo cells: 2219
 osteosarcoma, effect of estrogen or oophorectomy,
 rabbit: 2231
 c.c. tumors, effect of estrogen or orchiectomy,
 rat: 2264
 skin tumors, progressive loss of malignancy,
 mouse, review: 2157

 BENZANTHRACENE, 7,12-DIMETHYL-
 structure-activity relationship, proton
 magnetic resonance spectra: 2218
 thymic lymphoma, alkaline phosphatase, mouse:
 2389
 transplacental
 embryotoxicity, mouse: 2224
 review: 2128
 skin tumors, mouse: 2329
 11,12-BENZFLUORANTHRENE
 toxicity, mouse: 2237
 BENZFLUORANTHENE, 3:4,10:11,12:13-TRI-
 toxicity, mouse: 2237
 BENZIDINE
 aerosol, mammary tumors or leukemia, rat: 2233
 poisoning, rat: 2232
 BENZIDINE, N,N'-DIACETYL-
 poisoning, rat: 2232
 BENZIDINE, 3,3'-DICHLORO-
 poisoning, rat: 2232
 transplacental, effect on embryonic kidney
 or lung, mouse, review: 2128
 BENZIDINE, 3,3'-DIHYDROXY-
 poisoning, mechanism, rat: 2232
 BENZOFURAN, 3-AMINODI-
 bladder tumors, mouse: 2253
 BENZO(ghi)PERYLENE
 analysis, medicinal wax (ozokerite ceresin)
 from USSR: 2307
 metabolism, mouse embryo cells: 2219
 BENZOTRIAZOLE
 toxicity, rat or mouse: 2305
 3,4-BENZOPYRENE
 analysis
 air-borne dust, Switzerland, urban (Zurich)
 and rural: 2214
 medicinal wax (ozokerite ceresin) from USSR:
 2307
 petroleum refining products: 2211
 prunes, processing methods: 2215
 salt, processing methods: 2210
 smoked fish, processing methods: 2208, 2209
 soil and plants, airport area, USSR (Moscow):
 2212
 diesel oil containing, yeast culture medium,
 hydrocarbon biosynthesis: 2207
 distribution
 lung, effect of adsorption on asbestos or
 carbon black particles, hamster: 2201
 meat and milk, cows: 2216
 DNA binding, mechanism: 2206
 effect on liver microsomes, rat: 2204
 environmental, review: 2116
 excretion
 biliary, rat, liver microsomal enzymes: 2324
 rabbits, hens and cows: 2217
 hydroxylase, liver, strain differences, mice:
 2205
 lung tumors, mouse: 2199
 metabolism
 mammalian fibroblasts, species differences:
 2202
 mouse embryo cells: 2219
 osteosarcoma, rat: 2198, 2202
 skin tumors, mouse: 2237
 soil extracts containing, skin tumors, mouse:
 2213

- 3,4-BENZPYRENE, (Contd.)
 stomach tumors, effect of sucrose, saccharin or cyclamate, mouse: 2315
 structure-activity relationship, proton magnetic resonance spectra: 2218
 transplacental, lung tumors, mouse: 2329
- BERYLLIUM
 calcined beryllium oxides, toxicity (rodent) and lung tumors (rat): 2312
- BETEL
 chewing
 mouth cancer, case: 2313
 Papua/New Guinea: 2532
- BILIARY TRACT NEOPLASMS
 induction, Thorotrast, human: 2170, 2172
- BIPHENYL
 poisoning, rat: 2232
- BIPHENYL, N-HYDROXY-4-ACETYLAMINO-, SULFURIC ACID ESTER
 mutagenesis, bacteria: 2239
- N-4-BIPHENYLYLACETAMIDE, N-ACETOXY-
 synthesis: 2238
- BITTNER VIRUS (See under Virus, mammary tumor)
- BLADDER
 effect of sucrose, saccharin or cyclamate, mouse: 2315
- BLADDER CARCINOGENESIS
 aminodibenzofuran, mouse: 2253
 bracken extracts, rat: 2314
 ethylsulfonylnaphthalene-1-sulfonamide
 mouse: 2253
 rat: 2254
 fluorenylacetamide, mouse: 2253
 hydroxyfluorenylacetamide, age factors, rat: 2249
 β -naphthylamine, dog: 2236
 phenacetin abuse, human: 2545
 possible, cyclamates, U.S.: 2544
- BLADDER NEOPLASMS
 epidemiology
 artificial sweeteners including cyclamates, U.S.: 2544
 phenacetin abuse, Sweden (Gothenburg): 2545
 smoking, U.S.: 2544
 transitional cell carcinoma, exfoliative cytological diagnosis, standards: 2660
- BLOOD CELLS
 cell lines, cloning efficiency, chromosomes and herpes-type virus, normal subjects or pts. with non-malignant diseases: 2631
 RBC, nature of membrane polyoma virus receptors, human: 2466
- BLOOD GROUPS
 A, B and H antigens, mixed-cell agglutination reaction, lung cancer: 2626
 ABO, stomach cancer, Poland (Cracow): 2550
 haptoglobin and Gc group genotype, leukemia: 2595
- BLOOD PRESSURE
 effect of deoxycorticosterone, methylcholanthrene-induced tumors, rat: 2194
 Goldblatt-type hypertension, effect of methylcholanthrene, rat: 2193
- BLOOD PROTEINS
 effect of *o*-aminoazotoluene, mouse: 2234
 neoantigen, aflatoxin-induced, rat: 2293
- BLOOD PROTEINS, (Contd.)
 serum c-fetoprotein, liver or testicular tumors, human, review: 2134
- BONE
 osteomyelitis with fistula, skin cancer at fistula scar: 2158
- BONE NEOPLASMS
 induction
 benzpyrene, rat: 2198, 2200
 methylcholanthrene, rat: 2198
 nitroquinoline oxide, rat: 2198
 osteosarcoma
 dimethylbenzanthracene-induced, hormone effects, rabbit: 2231
 Moloney- or Harvey sarcoma virus-induced, rat or hamster: 2364
 radiation-induced, maxillary carcinoma, familial basal cell nevus syndrome: 2163
 sarcoma, mother and son, familial polyposis of colon: 2655
- BRACKEN (See *Pteridium aquilinum*)
- BRAIN
 astrocytes or choroid plexus cells, polyoma virus transformation, hamster: 2460
 effect of leukemia viruses, age factors, mouse: 2331
 immunity disorder, induction, syngeneic transplantable leukemia, mouse: 2331
 progressive multifocal leukoencephalopathy, polyoma virus-like particles, chronic leukemia, case: 2471
 short-wave irradiation and other CNS-acting treatment, effect on methylcholanthrene tumors, rat: 2192
 toxicity, cycasin, mouse: 2303
- BRAIN NEOPLASMS
 epidemiology
 Minnesota: 2579, 2580
 Poland (Cracow), temporal fluctuations: 2582
 South Africa (Transvaal), ethnic groups: 2581
 induction
 methylcholanthrene, pathology, mouse: 2189
 methylnitrosourea, effect of hyperestrogenism, rat: 2284
 enzymes, rat: 2269, 2270, 2283
 phenyldimethyltriazene, enzymes, rat: 2269, 2270
 simian adenovirus (SA-7), hamster: 2414
 transplacental ethylnitrosourea, enzymes, rat: 2283
- BREAST NEOPLASMS (See Mammary neoplasms, human)
- BROMODEOXYURIDINES (See under Antitumor agents)
- BRONCHUS NEOPLASMS
 cell growth kinetics, measurement method: 2614
 epidemiology, air pollution and smoking, East Germany: 2543
 scleroderma: 2153
- BURNS (See under Injuries or Scar tissue)
- BUSULFAN (See under Antitumor agents)
- CALCITONIN
 adrenal medulla, possible significance in multiple endocrine tumor syndrome (Type 2): 2651

- annabis
 alkaloids, effect on human WBC cultures: 2316
 ARBOHYDRATES
 transport, Harvey sarcoma virus-infected
 (hamster, human or mouse) or -transformed
 (rat) cells: 2360
 CARCINOGENESIS, CHEMICAL
 acylarylhydroxylamines, structure-activity
 relationship, rat: 2251
 cell growth kinetics, animal, review: 2127
 hamster cheek pouch, cell growth kinetics,
 review: 2125
 hormones, role of pituitary-adrenal system,
 review: 2120
 hydrocarbons, mechanism, review: 2123
 mechanism, review: 2122, 2155
 skin, mouse, review: 2124
 urethan, dimethylbenzanthracene or methyl-
 cholanthrene, hamster strain (Phodopus
sungorus): 2642
 CARCINOGENS, CHEMICAL
 bronchial epithelial cell abnormalities,
 classification: 2319
 effect on skin, intramitochondrial dense body,
 mouse: 2184
 environmental, liver cancer, international: 2561
 evaluation methods, mathematical model, review:
 2130
 teratogenesis, animal, review: 2129
 CLONAL BODY NEOPLASMS
 chemodectoma, familial bilateral, case and
 review: 2653
 CELL GROWTH KINETICS
 adenovirus 7- or SV40-adenovirus 7-transformed
 cells: 2470
 benign or malignant thyroid tumors, animal:
 2119, 2629
 breast cancer, free radical content: 2612
 cervix cancer, human: 2570, 2611
 chemical carcinogenesis, animal, review: 2125,
 2127
 cloning efficiency
 mouse lymphoma or plasmacytoma cells: 2640
 WBC cell lines from normal subjects or cancer
 pts.: 2631
 dimethylbenzanthracene mammary tumors, rat: 2228
 glutathione biosynthesis and carcinogenesis,
 review: 2122
 hepatoma-susceptibility genotype effects on
 liver, mouse: 2618, 2619, 2620
 human cancer, mathematical model: 2613, 2614,
 2615
 kidney, effect of mammary tumor virus in vitro,
 mouse: 2394
 lung, relation to urethan susceptibility, mouse
 or hamster: 2287
 Moloney sarcoma virus-infected or -transformed
 mouse cells: 2366
 mouse hepatomas of rapid or slow growth rate,
 circadian rhythm: 2617
 polyoma virus-transformed cells: 2470
 radiation carcinogenesis, animal, review: 2125,
 2126, 2127
 rat mammary gland, effect of estrus cycle: 2616
 rat sarcoma virus-infected cells: 2386
 CELL GROWTH KINETICS, (Contd.)
 Shope papilloma virus-induced tumors,
 rabbit: 2473
 SV40-transformed cells: 2436, 2470
 syngeneic or allogeneic host-mammary tumor
 systems, mouse: 2627
 thymus, radiation leukemia, mouse: 2164
 tumors induced by prenatal irradiation,
 latent periods, children: 2169
 viral carcinogenesis, animal, review: 2126
 CERESIN (See under Wax, medicinal)
 CERIUM HYDROXIDE
 dust, lung cancer, radon exposure, rat: 2171
 CERVIX UTERI NEOPLASMS
 cell line, karyotype: 2632
 epidemiology
 Canada: 2569, 2570
 effect of tubal-ligation sterilization,
 Puerto Rico: 2574
 India (Bhopal), ethnic groups: 2573
 Kentucky (Louisville), ethnic groups: 2571
 New Zealand, ethnic groups: 2572
 Poland (Bialystok province): 2624
 reproductive histories, U.S.: 2568
 serum herpesvirus-1 or -2 antibodies,
 Georgia (Atlanta): 2576
 USSR (Krivoi Rog), methods: 2575
 growth kinetics: 2570, 2611
 postoperative vaginal reconstruction,
 malignant transformation, case: 2658
 CHEEK POUCH NEOPLASMS
 dimethylbenzanthracene-induced
 antibody staining, hamster: 2229
 effect of antitumor agents, hamster: 2230
 premalignant, ultrastructure, hamster: 2225
 CHLORTETRACYCLINE
 skin tumor promotion, mouse: 2195
 CHROMOSOMES
 abnormalities, malignant lymphoma and myeloma,
 review: 2151
 acute leukemia, review: 2152
 autonomy and malignancy of induced thyroid
 tumors, rat: 2629
 chronic leukemia: 2635, 2636
 effect of Cannabis alkaloids, human WBC
 cultures: 2316
 HeLa cell lines: 2630
 hetero- and homotransplanted hamster or
 human tumors: 2664
 human cervix carcinoma cell line: 2632
 lymphoma, lymphocyte cultures: 2638
 L₂C guinea pig leukemia: 2633
 mouse lymphoma or plasmacytoma cell lines:
 2640
 peripheral WBC cell lines, human: 2631, 2662,
 2663
 plastic implanted tumors, mouse: 2300
 ploidy, growth kinetics, cervix cancer,
 human: 2611
 radiation-induced leukemia, Hiroshima: 2165
 sarcoma-inducing, spontaneously transformed
 rat embryo cell cultures: 2628
 sex
 mosaicism (XX/XXY), lung cancer, SV40
 transformation of WBC and fibroblast
 cultures: 2456

- CHROMOSOMES, (Contd.)
 sex, (contd.)
 uterine carcinoma: 2661
 SV40-transformed human cells: 2455
 transplantable sarcoma, strain differences,
 rat: 2665
 treated or untreated polycythemia vera: 2641
 trisomy-G, acute erythroleukemia, case: 2637
 CLAUDE'S CHICKEN TUMOR VIRUS 10 (See under Virus,
 sarcoma)
 CLUSTERING (See under Disease outbreaks)
 COLON
 familial polyposis
 associated bone sarcomas, mother and son:
 2655
 Gardner's and Turcot's syndrome: 2654
 COLON NEOPLASMS
 epidemiology
 appendectomy, West Germany: 2587
 California (Los Angeles), ethnic groups:
 2556
 familial polyposis: 2558, 2672
 Jamaica: 2557, 2622
 Tennessee (Nashville) ethnic groups: 2555
 CONNECTIVE TISSUE
 mesenchyme, development of transplanted
 mammary tumors, mouse: 2646
 CONNECTIVE TISSUE NEOPLASMS
 Gardner's syndrome type, associated familial
 colonic polyposis and Turcot's syndrome:
 2654
 muscle sarcoma, methylcholanthrene-induced,
 mouse: 2191
 CORPUS UTERI NEOPLASMS
 endometrium carcinoma, prognosis and
 histology: 2621
 epidemiology, Kentucky (Louisville): 2571
 growth kinetics, mathematical model: 2613
 sex chromosomes: 2661
 COUMARIN COMPOUND
 detergent additive, skin tumors, radiation
 effects, mouse: 2301
Crotalaria spectabilis
 pyrrolizidine alkaloid, liver toxicity, rat:
 2308
 CROTON OIL
 promotion of transplacental dimethylbenzanthra-
 cene skin tumors, mouse: 2329
 CROTON OIL PHORBOL ESTERS
 effect on radiation-induced skin damage, mouse:
 2299
 CUPRIC ACETATE
 effect on liver enzyme response to carcinogen,
 rat: 2260
 CYANURIC ACID (See s-Triazine-2,4,6-triol)
 CYCASIN
 liver tumors and reticulum cell sarcoma, mouse:
 2303
 toxicity, brain, mouse: 2303
 CYCLAMATES
 bladder cancer, U.S.: 2544
 effect on g.i. tract, mouse: 2315
 CYCLOHEXANE, HEXACHLORO-
 transplacental, effect on embryonic kidney or
 lung, mouse, review: 2128
 CYCLOPHOSPHAMIDE (See under Antitumor agents)
 DEFICIENCY, DIETARY
 iodine, with ¹³¹I, thyroid tumors, effect of
 hypophysectomy, rat: 2265
 DEOXYCORTICOSTERONE
 effect on blood pressure and growth of
 methylcholanthrene tumor rat: 2194
 DETERGENT ADDITIVES
 "brighteners," skin tumors, radiation effects,
 mouse: 2301
 DIABETES MELLITUS
 cancer epidemiology, Massachusetts: 2519
 DIENESTROL
 effect on dimethylbenzanthracene osteosarcoma,
 rabbit: 2231
 DIESEL EXHAUST PRODUCTS (See under Engine exhaust
 gases or Petroleum and petroleum products)
 DIETARY FACTORS (See also Foods)
 esophagus cancer, Jamaica and Australia,
 comparison: 2533
 leukemia, Europe, review: 2135
 thyroid cancer, world, review: 2133
 DIETHYLSTILBESTROL
 effect on dimethylaminoazobenzene or
 dimethylbenzanthracene tumors, rat: 2264
 DISEASE OUTBREAKS
 leukemia clusters
 Europe, review: 2135
 Japan: 2597, 2598, 2599, 2600
 DISEASE TRANSMISSION
 cellular, L₂C leukemia, guinea pig: 2634
 feline fibrosarcoma virus
 marmoset: 2504
 transplacental, kittens or puppies: 2392
 human leukemia
 mouse: 2502
 primates (baboons or macaques) virus-like
 particles: 2503
 liver carcinoma, human, to mouse: 2502
 Lucké herpes-type virus, horizontal or
 vertical, frog: 2493
 mouse leukemia viruses, horizontal, mouse: 2352
 Rous sarcoma virus, poultry farm to quail farm,
 USSR: 2382
 DISTRIBUTION
 aflatoxin B-1 and metabolites, mammals and
 birds: 2294
 benzpyrene
 dietary, meat and milk, cows: 2216
 rabbits, hens and cows: 2217
 lung, effect adsorption on carbon black
 or asbestos particles, hamsters: 2201
 beryllium oxides, effect of particle properties,
 rodent: 2312
 nitroquinoline oxide, *Tetrahymena pyriformis*:
 2275
²³⁹Pu, effect of oophorectomy, rat: 2299
 sugar transport, Harvey sarcoma virus-infected
 (hamster, human or mouse) or -transformed
 (rat) cells: 2360
 urethan, effect of partial hepatectomy, mouse:
 2285
 DUST
 air-borne, benzpyrene content, Switzerland,
 urban (Zurich) and rural: 2214
 carbon black, benzpyrene-adsorbed, effect on
 benzpyrene uptake by lung, hamster: 2201

- , (Contd.)
 erium hydroxide, combined with radon, lung
 tumors, rat: 2171
 erylum oxides, toxicity (rodent) and lung
 tumors (rat): 2312
 AND STAINS
 tarting material, liver or skin tumors, mouse
 or rat: 2272
- TRICITY
 effect on rat tumor: 2181
- YO
 idney, effect of transplacental dimethyl-
 benzanthracene, mouse: 2224
- CRINE ABLATION
 ypophysectomy
 effect on thyroid tumor induction (low-
 iodine diet + ^{131}I), rat: 2265
- phorectomy
 effect on
 dimethylbenzanthracene osteosarcoma,
 rabbit: 2231
 liver and hepatoma growth, hepatoma-
 susceptibility genotype, mouse: 2619
 ^{239}Pu distribution, rat: 2299
 transplantable mammary tumors, mouse:
 2267
- chiectomy
 effect on
 dimethylaminoazobenzene or dimethyl-
 benzanthracene tumors, rat: 2264
 liver and hepatoma growth, hepatoma-
 susceptibility genotype, mouse: 2619
 methylcholanthrene skin tumors, mouse:
 2197
 transplantable mammary tumors, mouse:
 2267
- RINE ORGAN NEOPLASMS
 renal and other glands, ^{239}Pu -induced, rat:
 2177
 itiple tumor syndrome (Type 2), pathogenesis,
 role of adrenal medullary calcitonin-like
 factor: 2651
- DIOXIN, BACTERIAL
 effect on methylcholanthrene tumors, rat: 2192
- GE EXHAUST GASES (See also Petroleum and
 Petroleum products; see also Air pollution)
 diesel fuel combustion products, salt-drying
 method, benzpyrene content: 2210
 icket exhaust, beryllium-containing, toxicity
 (rodents) and lung tumors (rat): 2312
 and plant benzpyrene contents, airport,
 USSR (Moscow): 2212
- ENVIRONMENTAL FACTORS
 cancer epidemiology, geographical variations,
 Kenya (western) and Tanzania (northwestern):
 2520
 Geographical variations
 larynx cancer, Ukrainian SSR: 2534
 leukemia, Japan: 2597, 2598, 2599, 2600
 lip cancer, U.S.: 2530
 stomach cancer, ethnic groups, Uzbekh SSR:
 2547
 Japan (Osaka and Nara prefectures): 2546
 Utah: 2552
 kemia epidemiology, Europe, review: 2135
- ENVIRONMENTAL FACTORS, (Contd.)
 liver cancer, international: 2561
 liver carcinogens, review: 2118
 seasons
 acute leukemia, children, Maryland (Baltimore):
 2590
 Hodgkin's disease, West Germany, urban and
 rural: 2606
 virus-positive kidney tumors, frogs,
 Minnesota: 2494
 urbanization
 benzpyrene content of air-borne dust,
 Switzerland (Zurich): 2214
 bronchitis, Great Britain: 2535, 2536
 cancer epidemiology, France: 2521
 Poland: 2524
 lung cancer, air pollution and smoking,
 Scotland: 2536
 stomach cancer, Rumania: 2515
- ENZYMES
 alkaline phosphatase
 methyl- or ethylnitrosourea-induced brain
 tumors, rat: 2283
 thymic lymphoma induced by 6-mercaptopurine
 (or virus derived from the tumor) or
 dimethylbenzanthracene, mouse: 2389
 aminopyrine demethylase
 effect of nickel carbonyl, rat liver or
 lung: 2310
 aspartate transcarbamylase
 dimethylbenzanthracene mammary tumors, rat:
 2228
 benzpyrene hydroxylase
 strain differences, mouse liver: 2205
 catalase
 liver, normal and tumor-bearing rat: 2652
 cytochrome P-420
 effect of methylcholanthrene, rat liver:
 2326
 endonuclease
 effect on SV40 DNA: 2506
 esterases
 serum, aflatoxin-induced hepatoma, rat: 2292
 glucose phosphorylation
 dimethylaminoazobenzene liver tumors, rat:
 2261
 lactate dehydrogenase and isoenzymes
 effect of carcinogen and cupric acetate,
 rat: 2260
 microsomal
 liver, biliary benzpyrene excretion, rat:
 2324
 monoamine oxidase or histaminase
 effect of benzdine and related compounds,
 rat: 2232
 phenyldimethyltriazene- or methylnitrosourea-
 induced brain tumors, rat: 2269, 2270
 RNA-dependent DNA polymerase
 Rous sarcoma (Schmidt-Ruppin) virions: 2388
 tetrahydrofolate dehydrogenase
 virus-induced leukemias, mouse: 2350
 transfer RNA-methylating, mouse or rat mammary
 tumors: 2647
- EPIDEMIOLOGY
 adeno-associated virus antibodies, cancer pts.,
 adults and children: 2589
 adenovirus antibodies, cancer pts.: 2588

EPIDEMIOLOGY, (Contd.)

- all tumors
 - appendectomy and/or tonsillectomy, New York (Kings County): 2586
 - Congo (Brazzaville): 2514
 - France, air pollution: 2521
 - occupational groups: 2522
 - high-risk diseases, children, review: 2137
 - international (14 nations): 2513
 - Kenya (western) and Tanzania (northwestern), geographical variations: 2520
 - Massachusetts, diabetes mellitus: 2519
 - newborn infants, U.S.: 2518
 - Nigeria (Ilesha township): 2523
 - Poland: 2524, 2525
 - Rumania: 2515, 2516
 - Switzerland (St. Gallen and Appenzell): 2526
 - USSR, urban: 2517
- bladder cancer
 - artificial sweeteners including cyclamates, U.S.: 2544
 - phenacetin abuse, Sweden (Gothenburg): 2545
- brain tumors
 - Minnesota: 2579, 2580
 - Poland (Cracow), temporal fluctuations: 2582
 - South Africa (Transvaal), ethnic groups: 2581
- breast cancer
 - England and Africa (Nigeria and Uganda), comparison of malignancy, genetic factors: 2562
 - methods: 2563
 - New York City: 2564
 - reproductive histories, Taiwan: 2567
 - and lactation, international: 2565
 - Japan (Tokyo): 2566
- bronchial cancer
 - air pollution and smoking, East Germany: 2543
- bronchitis
 - air pollution, data evaluation methods: 2537
 - Great Britain (including Scotland), air pollution and smoking: 2535, 2536
- Burkitt's lymphoma
 - Kenya (western) and Tanzania (northwestern): 2520
 - reovirus Type 3 and Epstein-Barr virus, review: 2138
 - sickle cell trait genotype, Uganda (Kampala): 2609
- cervix cancer
 - Canada: 2569, 2570
 - Georgia (Atlanta), serum herpesvirus-1 or -2 antibodies: 2576
 - India (Bhopal), ethnic groups: 2573
 - Kentucky (Louisville), ethnic groups: 2571
 - New Zealand, ethnic groups: 2572
 - Poland (Bialystok province): 2624
 - Puerto Rico, tubal-ligation sterilization: 2574
 - reproductive histories, U.S.: 2568
 - USSR (Krivoi Rog), methods: 2575
- colon/rectum cancer
 - California (Los Angeles), ethnic groups: 2556

EPIDEMIOLOGY, (Contd.)

- colon/rectum cancer, (Contd.)
 - Jamaica: 2557, 2622
 - Tennessee (Nashville), ethnic groups: 2555
- esophagus cancer
 - Jamaica and Western Australia, dietary factors: 2533
- familial polyposis of colon
 - risk of malignant transformation: 2558, 2672
- female genital tumors
 - New York (upstate): 2577
- g.i. cancer
 - Kenya (western) and Tanzania (northwestern): 2520
 - risk, effect of appendectomy, West Germany: 2587
- head and neck tumors
 - children, Sweden (Malmö): 2583
 - sunlight, Sweden: 2529
- Hodgkin's disease
 - hepatitis-associated (Australia) antigen distribution: 2591
 - relationship to multiple sclerosis, review: 2139
 - West Germany: 2606, 2607
- kidney cancer
 - phenacetin abuse, Sweden (Gothenburg): 2545
- larynx cancer
 - Ukrainian SSR (Kirovograd), occupation and geographical variations: 2534
- leukemia
 - Australia, rheumatic disorders: 2625
 - children, perinatal and congenital, twins, review: 2136
 - environmental factors, Europe, review: 2135
 - France, relationship to reproductive history: 2594
 - Georgia (Atlanta), ethnic groups: 2593
 - haptoglobin and Gc group genotype: 2595
 - hepatitis-associated (Australia) antigen distribution: 2591
 - Japan: 2596
 - correlation with other tumors: 2601
 - familial: 2605
 - geographical variations: 2597, 2598, 2599, 2600
 - radiation exposure, Hiroshima/Nagasaki: 2602, 2603
 - occupational or therapeutic: 2166, 2167, 2168, 2604
 - Maryland (Baltimore), children, seasonal onset: 2590
 - U.S. metropolitan areas, ethnic groups (Jews, Russians and Poles): 2592
- lip cancer
 - environmental factors (including smoking), U.S.: 2530
- liver tumors
 - Congo (Brazzaville): 2514
 - international, environmental factors (chemical and biological): 2561
 - Japan, cirrhosis and alcohol consumption: 2560
 - Hiroshima/Nagasaki: 2559
- lung cancer
 - air pollution, data evaluation methods: 2537
 - appendectomy, West Germany: 2587

DEMOLOGY, (Contd.)

lung cancer, (Contd.)

East Germany, air pollution and smoking:
2543

Japan (2 cities), air pollution and
smoking: 2538

occupational pneumoconiosis with/without
asbestosis: 2320, 2321

Scotland (urban and rural), air pollution
and smoking: 2536

smoking

California (San Diego), sex difference:
2541

Jews, Montreal: 2539

Pittsburgh: 2540

South Africa, ethnic groups: 2542

lymphoma

children, Israel, ethnic groups: 2610

Jamaica: 2608

West Germany: 2607

melanoma

U.S., age factors: 2528

mouth cancer

India (Madhya Pradesh), ethnic groups,
tobacco chewing: 2531

Papua/New Guinea, betel chewing: 2532

ovarian cancer

New York (upstate): 2577

salivary gland tumors

Sweden (Stockholm): 2584

secondary malignant tumors

risk, nevus sebaceus of skin: 2527

serum α -fetoprotein, liver tumors or embryonal

carcinoma of testis, review: 2134

skin cancer

head and trunk, Sweden, sunlight: 2529

small intestine tumors

Japan: 2554

Michigan (Detroit): 2553

stomach cancer

Armenian SSR (Yakutsk): 2548

geographical variations, Japan (Osaka and
Nara prefectures): 2546

Utah: 2552

Uzbekh SSR, ethnic groups: 2547

Yugoslavia: 2549

pernicious anemia, Minnesota (Minneapolis):
2551

Poland (2 cities): 2550, 2623

stomach tumors

Finland: 2578

thyroid cancer

radiation exposure, New York (Rochester):
2173

Switzerland (Lausanne): 2585

world, review: 2133

uterine cancer

Kentucky (Louisville): 2571

PHYSIOLOGY, VETERINARY

liver renal adenocarcinomas, fgs, Minnesota,
North Dakota and Louisiana: 2494

rabies sarcoma virus antibodies, domestic and
wild birds, USSR: 2382

testis tumors, possible genetic or viral

influence, Mexican axolotl (Ambystoma
mexicanum): 2650

EPSILON-AMINOCARPOIC ACID

effect on transplanted tumors, mouse: 2302

EPSTEIN-BARR VIRUS (See under Virus, herpes-
type)

EQUINE PAPILLOMA VIRUS (See under Virus, papova)

ESOPHAGUS NEOPLASMS

cell growth kinetics, measurement method: 2614
epidemiology

Australia and Jamaica, comparison, dietary
factors: 2533

Kenya (western) and Tanzania (northwestern):
2520

malignant transformation

of achalasia of cardia or chemical stricture:
2159, 2160

of marginal or pharynoesophageal diverticulum:
2669, 2670

ESTRADIOL BENZOATE

effect on transplantable mammary tumors, mouse:
2267

ESTROGENS

carcinogenic activity, role of pituitary-
adrenal system, review: 2120

hyperestrogenism, effect on methyl nitrosourea-
induced brain tumors, rat: 2284

ESTRUS CYCLE

effect on growth kinetics, rat mammary gland:
2616

ETHIONINE, DL-

effect on m-toluenediamine liver tumors, rat:
2235

ETHNIC GROUPS

brain tumors

Minnesota: 2579

South Africa (Transvaal): 2581

cervix cancer

India (Bhopal): 2573

Kentucky (Louisville): 2571

New Zealand: 2572

colon/rectum cancer

California (Los Angeles): 2556

Tennessee (Nashville): 2555

leukemia

aged, Georgia (Atlanta): 2593

U.S. metropolitan areas: 2592

lip cancer

U.S.: 2530

lung cancer

smoking, Montreal: 2539

Pittsburgh: 2540

South Africa: 2542

lymphoma

children, Israel: 2610

oral and pharyngeal cancer

tobacco chewing, India (Madhya Pradesh): 2531

stomach cancer

Uzbekh SSR: 2547

FATTY ACIDS, CYCLOPROPENOID

effect on aflatoxin hepatoma, trout: 2330

FEEDS, ANIMAL

aflatoxin content, products of African or
French origin: 2296

benzpyrene-containing

benzpyrene distribution in meat and milk,
cows: 2216

FEEDS, ANIMAL, (Contd.)

benzpyrene containing, benzpyrene, (Contd.)
excretion, rabbits, hens and cows: 2217

FLUORENE, 2-AMINO-

effect on liver microsomes, rat: 2240, 2241

N-2-FLUORENYLACETAMIDE

bladder tumors, mouse: 2253

DNA or RNA binding, mechanism, rat liver: 2243, 2244, 2245

hepatoma, pathology and metabolism, rat: 2247, 2248

protein binding, mechanism, rat liver: 2242

N-2-FLUORENYLACETAMIDE, N-ACETOXY-

decomposition pathways: 2238

effect on

liver microsomes, rat or guinea pig: 2241

RNA, bacteria: 2250

N-2-FLUORENYLACETAMIDE, N-HYDROXY-

DNA or RNA binding, mechanism, rat liver: 2244, 2246

liver, g.i. and bladder tumors, age factors, rat: 2249

protein binding, mechanism, rat liver: 2242

N-2-FLUORENYLACETAMIDE, N-HYDROXY-, ESTERS

mutagenesis, bacteria: 2239

FOOD PROCESSING METHODS

drying, benzpyrene content of prunes: 2215

fish smoking, benzpyrene content, gas combustion products: 2208

wood smoke: 2209

salt drying, benzpyrene content: 2210

FOODS (See also Dietary factors)

aflatoxin content, products of African or French origin: 2296

artificial sweeteners

bladder cancer, U.S.: 2544

effect on g.i. tract, mouse: 2315

fish, benzpyrene content, processing methods: 2208, 2209

milk from benzpyrene-fed cows, benzpyrene uptake by calves: 2216

prunes, benzpyrene content, drying methods: 2215

salt, benzpyrene content, processing methods: 2210

spinach, nitrosamine content, storage methods: 2278

FREE RADICALS

analysis, breast cancer, growth kinetics: 2612

FUNGI

effect of aflatoxins, review: 2121

GASOLINE (See under Engine exhaust gases or Petroleum and petroleum products)

GASTROINTESTINAL CARCINOGENESIS

bracken extracts, rat: 2314

crude corn oil, mouse: 2328

dimethylhydrazine, rat: 2273

hydroxyfluorenylacetamide, age factors, rat: 2249

methylcholanthrene, mouse: 2191

sucrose, saccharin or sodium cyclamate, negative results, mouse: 2315

s-triazine compounds, mouse or rat: 2272

GENETICS, ANIMAL

Friend leukemia virus susceptibility, mouse: 2336, 2339, 2340

hepatoma-susceptibility gene, liver and hepatoma growth rate, mouse: 2618, 2619, 2620

high-spontaneous tumor hamster strain (Phodopus sungorus): 2642

host immunity and Moloney viral sarcoma

development, NZW x NZB hybrid mice: 2367

lung tumor-resistant mouse strain (C57BL), methylcholanthrene effect on lung explants: 2188

mouse strains with high and low thyroidal ¹³¹I uptake: 2644

NZB mice

autoimmunity, virus-like particles: 2332

effect of Rauscher leukemia virus on autoimmunity: 2347

ovarian tumor-susceptible mouse strain, hormone metabolism and hair loss pattern: 2268

spontaneous mammary tumors, lung tumors and plasma cell lymphomas, PBA mouse strain: 2647

strain differences

adenovirus-12 or SA-7 tumors, hamster: 2412

benzpyrene hydroxylase activity, mouse liver: 2205

Friend leukemia virus infection, histocompatibility genotypes, mouse: 2343

group-specific leukemia viral antibodies, high- or low-leukemia mouse strains: 2348

karyotype of Yoshida sarcoma, rat: 2665

plastic implant tumors, mouse: 2300

radiation-induced ovarian tumors, mouse: 2178

Rous sarcoma virus-induced tumors, rat: 2373

s.c. tumors induced by surgical adhesives, rabbit: 2306

surface antigens, leukemias of C57BL and

other mouse strains: 2351

testis tumors, Mexican axolotl (Ambystoma mexicanum): 2650

tumor growth and immunity, syngeneic or allogeneic host-mammary tumor systems, mouse: 2627

GENETICS, CELLULAR

cell-associated factor required for infectious

RSV(0) synthesis, chick embryo cells: 2385

polyoma virus DNA as biochemical tool for studies of genetic regulation, mammalian cells, review: 2144

GENETICS, HUMAN

bilateral carotid body chemodectomas, familial, case and review: 2653

brain tumors, familial, Minnesota: 2580

diseases associated with cancer risk, children, review: 2137

familial basal cell nevus syndrome

radiation-induced maxillary cancer: 2163

familial polyposis of colon

associated bone sarcomas, mother and child: 2655

Gardner's and Turcot's syndromes: 2654

risk of malignant transformation: 2558, 267

haptoglobin and Gc group genotype, leukemia: 257

- ETICS, HUMAN, (Contd.)
 leukemia, familial, Japna: 2605
 or twins, chromosomes, review: 2152
 ovarian dysgerminomas, sisters (adolescents):
 2659
 perinatal and congenital leukemia, twins,
 review: 2136
 sickle cell trait genotype, Burkitt lymphoma,
 Uganda (Kampala): 2609
 ETICS, MICROBIAL
 Friend (strain F-S or F-B) leukemia virus,
 gene governing splenic focus formation: 2336
 mouse leukemia viruses, classification method:
 2353
 ETICS, POPULATION
 relative malignancy and occurrence of breast
 cancer, England and Africa (Nigeria and
 Uganda): 2562
 TAL NEOPLASMS
 herpes simplex virus, review: 2147
 TAL NEOPLASMS, FEMALE
 epidemiology, New York (Upstate): 2577
 MATHIONE
 biosynthesis, chemical carcinogenesis, review:
 2122
 AND NECK NEOPLASMS
 epidemiology
 children, Sweden (Malmö): 2583
 skin cancer, Sweden, sunlight: 2529
 ERIN
 effect on transplanted tumors, mouse: 2302
 ECTOMY (See under Liver)
 ICIDES
 effect on glycolysis, rat liver: 2263
 lin and g.i. tumors, mouse or rat: 2272
 INES
 carcinogenic activity, role of pituitary-
 adrenal system, review: 2120
 effect on dimethylbenzanthracene mammary tumors,
 rat: 2228
 tabolic status, ovarian tumor-susceptible
 mouse strain: 2268
 NE, SOMATOTROPIC
 effect on transplantable mammary tumors, mouse:
 2267
 ZINE, 1,2-DIMETHYL-
 testinal tumors, rat: 2273
 CARBONS
 biosynthesis, yeast culture grown on benzpyrene-
 containing diesel oil: 2207
 hanism of action, review: 2123
 CARBONS, POLYCYCLIC AROMATIC
 eakdown rate of carcinogenic and non-carcino-
 genic compounds, mouse embryo cells: 2219
 photosensitization: 2203
 CYLAMINE
 egenesis, bacteria: 2252
 CYLAMINE COMPOUNDS
 cylaryl derivatives, structure-carcinogenic
 activity relationship, mammary and other
 tumors, rat: 2251
 YSECTOMY (See under Endocrine ablation)
- IMMUNE SERUM
 effect on methylcholanthrene s.c. tumors, mouse:
 2183
 IMMUNITY
 cellular
 adenovirus 12-infected (human) cells or tumor
 (hamster or mouse) cells: 2407, 2408,
 2411
 adenovirus-SV40 hybrid-transformed cells:
 2419, 2421, 2423
 AKR mouse leukemia virus, immune virolysis:
 2335
 bovine adenovirus, hog kidney cells: 2402
 C57BL mouse leukemias: 2351
 CELO virus-induced hamster tumor or
 infected chick cells: 2415, 2511
 chick fibroblast-hamster Rous sarcoma
 heterokaryons, effect of inactivated
 Sendai virus: 2384
 dimethylbenzanthracene-induced cheek
 pouch tumors, hamster: 2229
 Friend leukemia virus-induced rat tumor:
 2341
 Gross leukemia virus-infected cells: 2505
 mammary tumor virus infection, mouse: 2399
 Marek's disease virus-infected chicken or
 duck cells or tissues: 2483, 2484, 2485
 Mazurenko virus leukemogenesis, mouse: 2354
 methylcholanthrene-transformed mouse
 prostate cells: 2185
 mouse tumors induced by adenoviruses-3,
 -12 or -14, cross-reacting tumor-specific
 transplantation antigens: 2401
 polyoma virus
 infected mouse cells: 2458
 mouse tumor cells: 2457
 transformed mouse cells: 2432
 Rous sarcoma virus-infected or transformed
 cells: 2374, 2380
 Shope fibroma virus-infected rabbit cells:
 2474
 SV40
 infected cells: 2449, 2450, 2509
 transformed cells: 2432, 2433, 2448
 tumor cells: 2433, 2448, 2507
 tumor immunity, primary autochthonous host,
 review (book): 2141
 virus-induced tumors, review: 2143
 host
 adenovirus 12-infected monkeys: 2406
 bovine adenovirus, hamster: 2402
 Burkitt lymphoma, review: 2148
 effect of Friend mouse leukemia virus on
 transplanted rat tumors, rat or mouse:
 2344, 2345
 Epstein-Barr and Lucké herpesviruses,
 comparison, rabbit: 2489
 group-specific viral antibodies, low- or
 high-leukemia mouse strains: 2348
 guinea pig L₂C leukemia: 2633
 hamster with CELO adenovirus-induced tumors:
 2416
 hepatitis-associated (Australia) antigen,
 leukemia or Hodgkin's disease: 2591

IMMUNITY, (Contd.)

host (Contd.)

- histocompatibility genotypes, Friend leukemia virus-infected mouse strains: 2343
- mammary tumor virus and embryonic antigens, mouse: 2396
- Marek's disease virus-infected chickens: 2484
- Mazurenko virus leukemogenesis, mouse: 2354
- methylcholanthrene sarcoma, radiation effects, mouse: 2196
- mixed-cell agglutination reaction and ABH antigens, lung cancer: 2626
- NZW x NZB hybrid mice with Moloney viral sarcoma: 2367
- relation to tumor growth, syngeneic or allogeneic host-mammary tumor systems, mouse: 2627
- Rous viral sarcoma, rat: 2373
- SA7(C8) simian adenovirus-induced tumor immunity, hamster: 2413
- serum antibodies
 - adeno-associated viruses, human cancer: 2589
 - adenovirus T antigens, human cancer: 2588
 - Epstein-Barr virus, mammals and frogs: 2493
 - pts. with infectious mononucleosis, Burkitt lymphoma or nasopharynx cancer: 2481
 - herpesvirus-1 or -2, cervix cancer, Georgia (Atlanta): 2576
 - polyoma tumor-specific surface antigens, mouse: 2457
 - Rous sarcoma virus, domestic and wild birds, USSR: 2382

SV40

- induced hamster tumors: 2431
- infected rabbit or monkey: 2428, 2440
- tumor immunity, primary autochthonous host, review (book): 2141

viral

- capsid antigens, herpes simplex and Epstein-Barr viruses: 2480

IMMUNITY DISORDERS

- autoimmunity
 - effect of Rauscher leukemia virus, NZB mice: 2347
 - virus-like particles, NZB mice: 2332
- CNS disease induced by syngeneic transplantable leukemia, age factors, mouse: 2331
- rheumatic type, leukemia incidence, Western Australia: 2625
- scleroderma, malignant transformation, case (bronchial cancer) and review: 2153
- systemic lupus erythematosus and dysgammaglobulinemia, with malignant lymphoma, case and review: 2639

IMMUNOSUPPRESSION

- adenovirus-16 or SV40, Sendai virus-infected hamster: 2418
- Friend leukemia virus, mouse: 2338
- Moloney sarcoma virus, mouse: 2370
- Rauscher leukemia virus, NZB mice: 2347

INJURIES (See also Scar tissue and Stress)

- birth, brain tumors, adults and children, Minnesota: 2580
- burn scar, malignant transformation (skin cancer): 2158, 2162
- chemical, esophagus, malignant transformation: 2159
- electricity, effect on induced (thyroid) or transplantable tumors, rat: 2181
- mechanical, skin cancer: 2158, 2657
- skin, intramitochondrial dense body, mouse: 2184

INSECTS

- Drosophila, mutagenesis, urethan metabolites: 2289

INTERFERON

- effect on Friend virus leukemogenesis, mouse: 2346

INTERFERON INDUCERS

- effect on viral carcinogenesis, review: 2140
- INTESTINE, LARGE, NEOPLASMS

- induction, dimethylhydrazine, rat: 2273

INTESTINE, SMALL, NEOPLASMS

epidemiology

- Japan: 2554
- Michigan (Detroit): 2553
- ileum or cecum, bracken extract-induced, rat: 2314
- induction, dimethylhydrazine, rat: 2273

IODINE DEFICIENCY

- with or without ¹³¹I, thyroid tumors, rat: 2265, 2266, 2629

IODINE, RADIOACTIVE (See under Radioactive isotopes and elements)

IRON

- plasma, normal and tumor-bearing rat: 2652

KIDNEY

- embryonic, effect of transplacental carcinogens, mouse: 2128, 2224

KIDNEY CARCINOGENESIS

- dimethylnitrosamine, rat: 2280
- lead acetate or nitrate, role of abnormal nucleolus, frog: 2309
- phenacetin abuse, human: 2545

KIDNEY NEOPLASMS

epidemiology

- phenacetin abuse, Sweden (Gothenburg): 2545
- Lucké adenocarcinoma (frog)
 - cytoplasmic virus particles: 2495
- epidemiology, Minnesota, North Dakota and Louisiana: 2494
- plasmacytoma in recipient, virus-like particles: 2496
- temperature effect on virus development: 2492

- viral latent period: 2490

- transitional cell carcinoma, exfoliative cytological diagnosis, standards: 2660

KUNITZ' PLASMIN INHIBITOR

- effect on transplanted tumors, mouse: 2302

ATION

history, breast cancer
 international: 2565
 Japan (Tokyo): 2566
 NX NEOPLASMS
 cell growth kinetics, measurement method: 2614
 epidemiology
 Ukrainian SSR (Kirovograd), occupation and
 geographical variations: 2534
 acetate or nitrate, lung and kidney tumors,
 role of abnormal nucleolus, frog: 2309
 LEMIA, EXPERIMENTAL (See also Virus, leukemia/
 lymphoma)
 avian myeloblastosis virus-induced, viral RNA
 and cellular DNA, chicken: 2378
 57BL mouse strain, surface antigens: 2351
 (AKR) leukemia (Gross leukemia virus-induced),
 effect of anticoagulants, mouse: 2302
 (mouse), immunization, CNS disease, age
 factors, mouse: 2331
 2C (guinea pig)
 cellular transmission, Strain 2 or hybrid
 guinea pig: 2634
 chromosomes, antigenicity and role of virus:
 2633
 spontaneous, effect of transplacental methyl-
 nitrosourea, AKR mice: 2282
 LEMIA, HUMAN
 acute
 erythroleukemia, G-trisomy in leukemia cells:
 2637
 myeloblastic, with infectious mononucleosis,
 serum Epstein-Barr virus antibodies,
 case: 2482
 cell lines
 chromosomes: 2631, 2663
 herpes-type virus, cloning efficiency: 2631
 Hs, effect on amphibians and reptiles: 2383
 chromosomes, review: 2152
 monoclonal lymphocytic
 chromosomes: 2636
 progressive multifocal leukoencephalopathy,
 polyoma virus-like particles: 2471
 monoclonal myeloid, prognostic significance of
 Ph¹ chromosome: 2635
 epidemiology
 children, high-risk diseases, review: 2137
 perinatal and congenital, twins, review:
 2136
 Europe, environmental factors, review: 2135
 France, reproductive histories: 2594
 Georgia (Atlanta), ethnic groups: 2593
 haptoglobin and Gc group genotype: 2595
 hepatitis-associated (Australia) antigen
 distribution: 2591
 Japan: 2596
 correlation with other tumors: 2601
 familial: 2605
 geographical variations: 2597, 2598,
 2599, 2600
 radiation exposure, Hiroshima/Nagasaki:
 2602, 2603
 occupational or therapeutic: 2166,
 2167, 2168, 2604

LEUKEMIA, HUMAN, (Contd.)
 epidemiology, (Contd.)
 Maryland (Baltimore), children, seasonal
 onset: 2590
 rheumatic disorders, Western Australia:
 2625
 U.S. metropolitan areas, ethnic groups
 (Jews, Russians and Poles): 2592
 transmission
 baboons or macaques, virus-like particles:
 2503
 mice: 2502
 virus etiology, review: 2146
 LEUKEMOGENESIS, EXPERIMENTAL (See also Radiation
 leukemogenesis, experimental)
 benzidine, rat: 2233
 cycasin, mouse: 2303
 dimethylbenzanthracene, thymic lymphoma,
 alkaline phosphatase, mouse: 2389
 ethylnitrosourea, mouse: 2282
 6-mercaptopurine, thymic lymphoma, primary
 and virally-transmitted tumors, alkaline
 phosphatase, mouse: 2389
 photographic emulsion component or developing
 agent, mouse: 2305
 resin intermediates of acetone or phenol
 production, mouse: 2304
 tobacco lead powder, mouse: 2118
 urethan
 effect of leukemia virus, mouse: 2288
 partial hepatectomy, mouse: 2286
 LEUKOSIS, AVIAN
 Marek's disease virus, review: 2149, 2150
 LEUKOSIS, BOVINE
 exposure, leukemia epidemiology, Europe, review:
 2135
 LEUKOVIRUS (See under Virus, herpes-type)
 LIP NEOPLASMS
 epidemiology, environmental factors, U.S.: 2530
 herpes simplex virus, review: 2147
 LIVER
 benzpyrene hydroxylase, strain differences,
 mice: 2205
 biliary benzpyrene excretion, rat: 2324
 catalase, normal and tumor-bearing rat: 2652
 DNA
 effect of methyl dimethylaminoazobenzene,
 rat: 2256
 hydroxyfluorenylacetamide binding, rat:
 2244, 2246
 enzymes
 effect of
 dimethylaminoazobenzene and cupric
 acetate, rat: 2260
 nickel carbonyl, rat: 2310
 glycolysis and regulating enzymes, effect of
 herbicide, rat: 2263
 growth rate, hepatoma-susceptibility genotype,
 mouse: 2618, 2619, 2620
 microsomes
 effect of
 carcinogens, 2204, 2220, 2240, 2241, 2324,
 2326
 non-carcinogenic amine (dimethylaniline),
 rat: 2240, 2241

LIVER, (Contd.)

nucleoproteins, effect of methylcholanthrene, rat: 2325
partial hepatectomy, effect on urethan metabolism or tumor induction, mouse: 2285, 2286
proteins
effect of o-aminoazotoluene, mouse: 2234
fluorenylacetamide or hydroxyfluorenylacetamide binding, rat: 2242

RNA

effect of methyltrimethylaminoazobenzene, rat: 2255
fluorenylacetamide or hydroxyfluorenylacetamide binding, rat: 2243, 2244

m-toluenediamine uptake, effect of other carcinogens, rat: 2235

toxicity

aflatoxin, monkey: 2298
pyrrolizidine alkaloid, rat: 2308
retorsine, monkey: 2298
steritomatocystin, monkey: 2298

LIVER CARCINOGENESIS

aflatoxin

effect of cyclopropenoid fatty acids, trout: 2330

rat: 2292, 2295

avian adenovirus (CELO), hamster: 2511

cycasin, mouse: 2303

dimethylaminoazobenzene (rat): 2258, 2259, 2261, 2262, 2263, 2264

review: 2154

fluorenylacetamide, rat: 2247, 2248

hydroxyfluorenylacetamide, age factors, rat: 2249

mechanism, theory, human: 2561

methyltrimethylaminoazobenzene (rat)

effect of

noise: 2180

rotary motion: 2179

review: 2154

radiation, mouse: 2178

review: 2118

thioacetamide, rat: 2263

tobacco leaf powder, mouse: 2318

m-toluenediamine, effect of other carcinogens, rat: 2235

s-triazine compounds, mouse or rat: 2272

urethan

effect of leukemia virus, mouse: 2288

partial hepatectomy, mouse: 2286

LIVER DISEASES

cirrhosis

dimethylnitrosamine induction, dog: 2279
with/without hepatoma, alcohol consumption, Japan: 2560

hepatitis, associated (Australia) antigen distribution, leukemia or Hodgkin's disease: 2592

LIVER NEOPLASMS

epidemiology

Congo (Brazzaville): 2514

international, environmental factors (chemical and biological): 2561

Japan, cirrhosis and alcohol consumption: 2560

Hiroshima/Nagasaki: 2559

LIVER NEOPLASMS, (Contd.)

genetic susceptibility, liver and tumor

growth kinetics, mouse: 2618, 2619, 2620

growth kinetics, circadian rhythm, mouse: 2617

human, transmission to mouse: 2502

serum α -fetoprotein, review: 2134

LUCKÉ TUMOR (See under Kidney neoplasms)

LUCKÉ VIRUS (See under Virus, herpes-type)

LUNG

benzpyrene uptake, effect of adsorption on carbon black or asbestos particles, hamster: 2201

cultures, polyoma- or myxovirus-immunized hamsters, tumor-inducing capacity: 2462

effect of methylcholanthrene in vitro, lung tumor-resistant mouse strain: 2188

embryonic

effect of transplacental carcinogens, mouse, review: 2128

urethan or hydroxyurethan cytotoxicity in vitro, mouse: 2290

enzymes, effect of nickel carbonyl, rat: 2310

postnatal cellular proliferation, urethan susceptibility, mouse or hamster: 2287

toxicity

beryllium and beryllium-containing rocket exhaust products, rat: 2312

tobacco smoke, measurement method, mouse: 2317

LUNG CARCINOGENESIS

benzpyrene

mouse: 2199

transplacental, mouse: 2329

beryllium and beryllium-containing rocket exhaust products, rat: 2312

cerium hydroxide dust and radon, rat: 2171

lead acetate or nitrate, role of abnormal nucleolus, frog: 2309

methylcholanthrene

mouse: 2199

s.c. lung transplants, age factors, mouse: 2187

²³⁹Pu, rat: 2176, 2177

radiation, mouse: 2178

tobacco leaf powder, mouse: 2318

urethan

effect of

influenza virus, mouse: 2291

leukemia virus, mouse: 2288

partial hepatectomy, mouse: 2286

relation to postnatal cellular proliferation mouse or hamster: 2287

LUNG DISEASES

occupational, lung cancer, Japan: 2320, 2321

LUNG NEOPLASMS

associated XX/XXY mosaicism (Klinefelter's syndrome), SV40 transformation of WBC and fibroblast cultures: 2456

bronchogenic carcinoma, growth kinetics, mathematical model: 2615

epidemiology

air pollution, data evaluation methods: 253

blood groups (A, B and H antigens) and mixed

cell agglutination reaction: 2626

California (San Diego), smoking, sex

difference: 2541

UNG NEOPLASMS, (Contd.)

epidemiology, (Contd.)

- East Germany, air pollution and smoking: 2543
- Japan, air pollution and smoking, 2 cities: 2538
 - occupational pneumoconiosis with/without asbestosis: 2320, 2321
- Massachusetts, diabetes mellitus: 2519
- Montreal, smoking, Jews: 2539
- Pennsylvania (Pittsburgh), smoking, Jews: 2540
- Scotland (urban and rural), air pollution and smoking: 2536
- South Africa, smoking, ethnic groups: 2542
- West Germany, appendectomy: 2587
- incidence, high-tumor PBA mouse strain: 2643

MPHATIC TISSUE

MPHOMA, MALIGNANT, EXPERIMENTAL

- 6-mercaptopurine- or dimethylbenzanthracene-induced, alkaline phosphatase, mouse: 2389
- oil-induced, cloning efficiency and karyotype *in vitro*, mouse: 2640
- reticulum cell sarcoma, cycasin-induced, mouse: 2303

MPHOMA, MALIGNANT, HUMAN

- associated systemic lupus erythematosus and dysgammaglobulinemia, case and review: 2639
- Burkitt type 1
 - cell lines
 - chromosomes: 2663
 - virus-free, EB virus DNA homology: 2479

epidemiology

- Kenya (western) and Tanzania (north-western): 2520
- sickle cell trait genotype, Uganda (Kampala): 2609
- Epstein-Barr and reovirus Type 3, review: 2138
- host immunity and herpes-type virus, review: 2148
- serum Epstein-Barr virus antigens: 2481
- virus-like particles, biopsy specimens: 2478

- cell lines, cloning efficiency, chromosomes and herpes-type virus: 2631

chromosomes, review: 2151

epidemiology

- abdominal lymphomas, children, Israel, ethnic groups: 2610
- Jamaica, comparison with Africa: 2608
- West Germany: 2607
- Hodgkin's disease
 - epidemiology
 - hepatitis-associated (Australia) antigen distribution: 2591
 - West Germany: 2606
 - relationship to multiple sclerosis, review: 2139

- lymphocyte cultures, chromosomes: 2638

- small intestine, epidemiology, Michigan (Detroit): 2553

- virus etiology, review: 2146

MALIGNANT TRANSFORMATION

- achalasia of cardia or chemical stricture to cancer of esophagus: 2159, 2160
- calcifying Malherbe's epithelioma of skin, case: 2657
- carcinoma of pharyngoesophageal diverticulum, cases: 2670
- chronic ulcer to carcinoma, leg: 2666
- epidermodysplasia verruciformis to carcinoma of skin, verruca vulgaris virus particles, case: 2501
- epithelial nevus to melanoma, skin: 2671
- familial polyposis to cancer of colon: 2558, 2672
- fibroadenoma to malignant cystosarcoma phyllodes of breast: 2668
- marginal diverticulum to cancer of esophagus: 2669
- scar tissue to skin cancer: 2158, 2162
- scleroderma, case (bronchial cancer) and review: 2153
- spontaneous, rat embryo cell cultures, karyotype: 2628
- vaginal reconstruction (cervix cancer surgery), primary carcinoma of artificial vagina: 2658

MAMMARY CARCINOGENESIS, EXPERIMENTAL

- N-acetylarylhydroxylamines, structure-activity relationship, rat: 2251
- benzidine, rat: 2233
- dimethylbenzanthracene, rat: 2226, 2227, 2228
- ethylnitrosourea, mouse: 2282

MAMMARY GLAND

- growth kinetics, estrus cycle, rat: 2616

MAMMARY NEOPLASMS, EXPERIMENTAL (See also Virus, mammary)

- Adenocarcinoma 755 (mouse)
 - mammary tumor virus particles: 2395
- effect of immunosuppression, syngeneic or allogeneic host-tumor systems, mouse: 2627
- mouse or rat, transfer RNA-methylating enzymes: 2647
- rat tumor induced by Moloney sarcoma virus, pathology: 2368
- spontaneous
 - mouse, properties of DNA: 2648
 - role of virus, PBA mouse strain: 2643
 - transplantability, role of connective tissue, mouse: 2646
- transplanted, prolactin- or growth hormone-enhanced, mechanism, mouse: 2267

MAMMARY NEOPLASMS, HUMAN

epidemiology

- England and Africa (Nigeria and Uganda), comparison of malignancy, genetic factors: 2562
- methods: 2563
- New York City: 2564
- relationship to leukemia, Japan: 2601
- reproductive history and lactation
 - international: 2565
 - Japan (Tokyo): 2566
 - Taiwan, reproductive histories: 2567
- growth kinetics, free radical content: 2612
- leukemia incidence after radiotherapy, Japan: 2168

- MAREK'S DISEASE (See also under Virus, herpes-type)
 cell-free transmission, chick: 2486
 viral etiology, review: 2149, 2150
 virus-specific antigens and cell-free virus, infected or tumor-bearing chickens: 2484
- MELANOMA, MALIGNANT
 epidemiology, U.S., age factors: 2528
 transplantable (mouse or hamster), separation of viable tumor cells: 2645
- 6-MERCAPTOPYRINE (See also under Antitumor agents)
 thymic lymphoma, viral transmission, enzymes, mouse: 2389
- METABOLISM (glycolysis and respiration)
 effect of hepatocarcinogens, rat liver: 2263
 glycolysis, dimethylaminoazobenzene or transplanted hepatomas, rat: 2262
- METAPROTERENOL
 effect on tobacco smoke-induced ciliostasis, rabbit trachea *in vitro*: 2323
- METHOTREXATE (See under Antitumor agents)
- 3-METHYLCHOLANTHRENE
 brain tumors, pathology, mouse: 2189
 carcinogenic effect, hamster strain (*Phodopus sungorus*): 2642
 effect on
 cytochrome P-420, rat liver: 2326
 dimethylbenzanthracene metabolism, rat liver microsomes: 2220
 Goldblatt-type hypertension, rat: 2193
 liver nucleoproteins, rat: 2325
 lung explants from lung tumor-resistant mouse strain: 2188
 m-toluenediamine liver tumors, rat: 2235
 lung tumors, mouse: 2199
 mechanism of action, review: 2155
 muscle tumors
 circadian changes of body temperature, liver catalase and plasma iron, rat: 2652
 mouse: 2191
 osteosarcoma, rat: 2198
 s.c. tumors
 deoxycorticosterone effect on blood pressure, rat: 2194
 effect of
 CNS-acting treatment, rat: 2192
 immune serum, mouse: 2183
 host immunity and radiation effects, mouse: 2196
 leukemia virus group-specific antigen, mouse or rat: 2348
 rat: 2190
 skin tumors (mouse): 2156, 2182, 2184, 2191, 2195, 2197
 specific carcinogen-binding skin protein, mouse: 2221
 stomach tumors, mouse: 2191
 transformed mouse prostate cells, transplantation antigens: 2185
 tumor induction in s.c. lung transplants, age factors, mouse: 2187
- MONOCROTALINE
 liver toxicity, rat: 2308
- MONURON (See Urea, 3-(p-chlorophenyl)-1,1-dimethyl-)
- MOTION, ROTATORY (See under Stress)
- MOUTH NEOPLASMS
 betel chewing, case: 2313
 epidemiology
 India (Madhya Pradesh), ethnic group, tobacco chewing: 2531
 Papua/New Guinea, betel chewing: 2532
- MULTIPLE SCLEROSIS
 relationship to Hodgkin's disease, review: 2139
- MUSCLE
 cultures, differentiation, effect of dimethylbenzanthracene, rat: 2222
- MUSCLE NEOPLASMS (See under Connective tissue neoplasms)
- MUTAGENESIS
 N-hydroxy-aromatic amide esters, bacteria: 2239
 hydroxylamine, bacteria: 2252
 radiation, Rous sarcoma virus (Schmidt-Ruppin strain), chick embryo: 2381
 urethan metabolites, *Drosophila*: 2289
- Mycoplasma*
 infection, effect on SV40-transformed cells: 2510
- MYELOMA AND RELATED DISEASES
 cell lines
 chromosomes, human: 2663
 cloning efficiency, chromosomes and herpes-type virus: 2631
 chromosomes, human, review: 2151
 frog plasmacytoma, virus-like particles: 2496
 plasma cell lymphoma, incidence, high-tumor (PBA) mouse strain: 2643
 transplantable plasmacytomas, cloning efficiency and karyotype *in vitro*, mouse: 2640
- NAPHTHALENE-1-SULFONAMIDE, 4-ETHYLSULFONYL-
 bladder tumors
 mouse: 2253
 pathogenesis, rat: 2254
- β -NAPHTHYLAMINE
 bladder tumors, dog: 2236
- NASAL CAVITY NEOPLASMS
 snuff taking, historical review: 2115
- NASOPHARYNX NEOPLASMS
 serum Epstein-Barr virus antigens: 2481
- NEOPLASMS, EXPERIMENTAL
 Adenocarcinoma #755 (mouse)
 mammary tumor virus particles: 2395
 amphibian tumors (frogs and newts)
 isolation and properties of cytoplasmic virus: 2497
 BP8 tumor (mouse; carcinogen-induced)
 effect of anticoagulants: 2302
 Ehrlich carcinoma (mouse)
 virus-induced fusion with L cells, properties and malignancy (mice) of hybrid cells (LE strain): 2499
 hamster
 hetero- or homotransplanted, chromosomes: 2664
 HeLa cell lines
 chromosomes: 2630

- OPLASM, EXPERIMENTAL, (Contd.)
 Morris hepatoma (rat)
 glycolysis: 2262
 mouse
 surface antigens: 2351
 Rous virus-induced hamster tumor clone #9
 ultrastructure: 2375
 Sarcoma 37 (mouse)
 stimulation, hepatoma-susceptibility
 genotype, mouse: 2620
 Sarcoma 180 (mouse)
 Friend leukemia virus replication: 2342
 spontaneous
 hamster carcinoma, properties of DNA: 2648
 multiple, male hamster, case and review:
 2649
 occurrence, hamster strain (Phodopus
 sungorus): 2642
 transplantable
 mouse or hamster melanomas, separation of
 viable tumor cells: 2645
 rat tumors, effect of Friend leukemia virus,
 mouse or rat: 2344, 2345
 tumor immunity, primary autochthonous*host,
 review (book): 2141
 Walker 256 carcinosarcoma (rat)
 effect of electrical injury: 2181
 effect on diurnal change in body temperature,
 liver catalase and plasma iron, rat: 2652
 growth kinetics, mathematical model: 2615
 Yoshida sarcoma (rat)
 chromosomes, strain differences: 2665
- PLASMS, HUMAN
 epidemiology
 Congo (Brazzaville): 2514
 France, occupational groups: 2522
 high-risk diseases, children, review: 2137
 international (14 nations): 2513
 Kenya (western) and Tanzania (northwestern),
 geographical variations: 2520
 newborn infants, U.S.: 2518
 Nigeria (Ilesha township): 2523
 Poland, urban and rural: 2524, 2525
 Rumania: 2515, 2516
 Switzerland (St. Gallen and Appenzell): 2526
 USSR, urban: 2517
 growth kinetics, mathematical model: 2613
 hetero- or homotransplanted, chromosomes: 2664
 multiple endocrine neoplasia Type 2 syndrome,
 pathogenesis, adrenal medullary calcitonin-
 like factor: 2651
 possible viral etiology, review: 2142
 risk, appendectomy and/or tonsillectomy, New
 York (Kings County): 2586
 serum antibodies
 adenovirus T antigens: 2588
 adenovirus-associated virus Types 1, 2 and
 3, adults and children: 2589
- ROUS SYSTEM NEOPLASMS
 urcot's syndrome type, associated familial
 colonic polyposis and Gardner's syndrome:
 syndrome: 2654
- ROUS SARCOMA
 relationship to von Recklinghausen's disease,
 child: 2656
- NICKEL CARBONYL
 effect on enzymes, rat liver or lung: 2310
 4-NITROQUINOLINE 1-OXIDE
 charge-transfer interactions with methyl-
 substituted benzene or aniline compounds:
 2277
 interaction with DNA, cell-free system: 2276
 osteosarcoma, rat: 2198
 uptake, Tetrahymena pyriformis: 2275
 4-NITROQUINOLINE 1-OXIDE, 6-CARBOXY-
 transformed cells inducing s.c. tumors, hamster:
 2274
 NITROSAMINE, DIMETHYL-
 kidney tumors, pathology, rat: 2280
 liver cirrhosis, dog: 2279
 NITROSAMINE COMPOUNDS
 analysis, spinach: 2278
 NITROSO COMPOUNDS
 transplacental carcinogenesis, embryonic kidney
 or lung explants, mouse, review: 2128
 N-NITROSOGUANIDINE, N-METHYL-N'-NITRO-
 effect on DNA, mechanism, normal cells: 2281
 N-NITROSOUREA, N-ETHYL
 effect on spontaneous tumor incidence, line A
 mice: 2282
 transplacental tumor induction, brain, rat:
 2283
 N-NITROSOUREA, N-METHYL-
 brain tumors, rat: 2269, 2270, 2283, 2284
 transplacental, effect on spontaneous leukemia
 incidence, AKR mice: 2282
 NOISE (See under Stress)
 NUCLEIC ACIDS, DNA
 adenovirus
 induced tumors or transformed cells, review:
 2145
 infected cells: 2400, 2512
 avian myeloblastosis virus-induced leukemia,
 chicken: 2378
 cell growth kinetics, human cancer: 2614
 rat mammary tumor: 2228
 carcinogen binding, mechanism: 2206, 2223
 effect of carcinogens
 bacteria: 2239
 cell-free system: 2276
 mouse bladder: 2253
 normal cells: 2281
 rat liver: 2235, 2244, 2245, 2246, 2256
 frog virus 3-infected human tumor cells: 2498
 from Agrobacterium tumefaciens phage, plant
 tumors: 2500
 hamster or mouse tumors, properties: 2648
 mammary tumor virus-infected mouse cells: 2394
 Marek's disease virus-infected duck embryo
 cells: 2488
 photosensitization by carcinogens: 2203
 polyoma virus
 biochemical tool for study of cellular
 genetics, review: 2144
 infected mouse cells: 2463, 2464, 2467
 ultrastructure: 2465
 radiation-induced leukemia, mouse: 2164
 RNA-dependent DNA polymerase, Rous sarcoma
 (Schmidt-Ruppin) virions: 2388
 Rous sarcoma virus

NUCLEIC ACIDS, DNA, (Contd.)

Rous sarcoma virus, (Contd.)

infected or transformed chick embryo cells: 2386

tumor cells, chick: 2648

Shope fibroma virus-infected rabbit cells, effect of contact inhibition or radiation: 2475

Shope papilloma virus-induced rabbit tumors: 2473

SV40

cleavage, bacterial endonuclease: 2506

effect on SV40-transformed mixed human-mouse cell cultures: 2434

infected monkey kidney cells: 2400, 2437, 2439, 2446, 2447

transformed cells: 2435, 2446, 2451

thermosensitive mutant (Ts-a) polyoma virus-transformed mouse cells: 2469

"virus-free" Burkitt lymphoma cell line: 2479

Yaba poxvirus-infected monkey kidney cells: 2477

NUCLEIC ACIDS, RNA

adenovirus-induced tumors or transformed cells, review: 2145

adenovirus-SV40 hybrid-transformed hamster cells: 2424

avian myeloblastosis virus-infected or leukemic cells, chick: 2377, 2378

dependent DNA polymerase, Rous sarcoma (Schmidt-Ruppin) virions: 2388

dimethylaminoazobenzene hepatoma, rat: 2258

dimethylbenzanthracene mammary tumors, growth rate, rat: 2228

effect of carcinogens

bacteria: 2250, 2252

mouse bladder: 2253

rat liver: 2235, 2243, 2244, 2245, 2255

frog virus 3-infected human tumor cells: 2498

from Rous sarcoma virus (Carr-Zilber strain), tumor induction, mouse: 2371

RNase susceptibility, effect of immune virolysis,

AKR mouse leukemia virus: 2335

Rous sarcoma virus-infected or -transformed

chick embryo cells: 2386

SV40-transformed cells: 2451

transfer RNA-methylating enzymes, mouse or rat mammary tumors: 2647

NUCLEIC ACIDS, RNA, SYNTHETIC POLYNUCLEOTIDE

effect on viral carcinogenesis, review: 2140

NUCLEOLUS

abnormalities, lead salt-induced kidney or lung tumors, frog: 2309

morphology, transitional cell carcinoma of bladder or renal pelvis: 2660

NUCLEOPROTEINS

effect of methylcholanthrene, rat liver: 2325

NUCLEUS

ultrastructure, adenovirus 5-infected human tumor cells: 2404

OCCUPATIONAL DISEASES

acetone and phenol production, carcinogenic effects (animals) of intermediate pyrolytic resins: 2304

OCCUPATIONAL DISEASES, (Contd.)

cancer and heart disease risk, France: 2522

larynx cancer, farmers and other groups, Ukrainian SSR: 2534

pneumoconiosis with/without asbestosis, lung cancer, Japan: 2320, 2321

radiation exposure, leukemia, Japan: 2166, 2167

stomach cancer, mining region of Utah: 2552

toxoplasmosis, farmers, brain tumors, Minnesota: 2579

OILS, EDIBLE

crude corn oil, stomach tumors, mouse: 2328

OOPHORECTOMY (See under Endocrine ablation)

ORCHIECTOMY (See under Endocrine ablation)

OVARY NEOPLASMS

dysgerminoma, bilateral, adolescent sisters: 2659

epidemiology

New York (upstate): 2577

relationship to leukemia, Japan: 2601

genetically susceptible mouse strain, hair loss patterns: 2268

radiation induction, strain difference, mouse: 2178

OZOKERITE (See under Wax, medicinal)

PANCREAS NEOPLASMS

epidemiology, Massachusetts, diabetes mellitus: 2519

PARASITES

infection, liver tumors, international: 2561

PERYLENE

analysis medicinal wax (ozokerite ceresin) from USSR: 2307

metabolism, mouse embryo cells: 2219

PETROLEUM AND PETROLEUM PRODUCTS (See also Air

pollution and Engine exhaust gases)

additives of medicinal wax (ozokerite ceresin) from USSR, carcinogen content: 2307

diesel oil

benzpyrene-containing, yeast culture, hydrocarbon synthesis: 2207

combustion products, salt-drying method, benzpyrene content: 2210

fuel consumption, air pollution, cancer

epidemiology, France: 2521

gas combustion products, effect on benzpyrene content of fish: 2208

refinery, benzpyrene content of soil, bioassay (mouse skin): 2213

refining products, benzpyrene content: 2211

soil contamination, benzpyrene content of soil and plants, airport, USSR (Moscow): 2212

PHARYNGOESOPHAGEAL DIVERTICULUM

malignant transformation, cases: 2670

PHARYNX NEOPLASMS

epidemiology, India (Madhya Pradesh), ethnic groups, tobacco chewing: 2531

PHENACETIN

abuse, bladder or kidney cancer, Sweden (Gothenburg): 2545

PHENANTHRENE, N-HYDROXY-2-ACETYLAMINO-, ACETIC ACID ESTER

mutagenesis, bacteria: 2239

- 12-PHENANTHRYLACETAMIDE, N-ACETOXY-
 synthesis: 2238
- ENIDONE (See 3-Pyrazolidinone, 1-phenyl-)
- ENOL
 production, intermediate pyrolytic resins, skin
 tumors and leukemia, animal: 2304
- PHORBOL ESTERS (See Croton oil phorbol esters)
- PHOTOGRAPHIC FILM
 emulsion component or developing agent,
 toxicity, rat or mouse: 2305
- ADRENAL SYSTEM
 hormonal carcinogenesis, review: 2120
 stimulation by stress, effect on methyl dimethyl-
 aminoazobenzene liver tumors, rat: 2179,
 2180
- ANT NEOPLASMS
 induction, *Agrobacterium tumefaciens* phage
 DNA: 2500
- ANTS
 benzpyrene content, airport area, USSR (Moscow):
 2212
- ASTICS (See also Polymers)
 s.c. tumors
 karyotype, strain and sex differences,
 mouse: 2300
 mechanism of induction, rat, review: 2117
 radiation effects, rat or dog: 2299
- CYTHERIA VERA
 treated or untreated, chromosomes: 2641
- YMERS
 methyl 2-cyanoacrylates (surgical adhesives),
 s.c. tumors, strain differences, mouse:
 2306
- YOMA VIRUS (See under Virus, papova)
- GNANCY
 effect of
 transplacental dimethylbenzanthracene on
 embryonic kidney, mouse: 2224
 methyl nitrosourea on leukemia incidence,
 AKR mice: 2282
- renatal radiation exposure, cancer latent
 periods, children: 2169
- reproductive histories
 breast cancer, international: 2565
 Japan (Tokyo): 2566
 Taiwan: 2567
 cervix cancer, U.S.: 2568
 leukemia risk, France: 2594
- ransplacental carcinogenesis
 benzpyrene, lung, mouse: 2329
 cat fibrosarcoma virus, kittens or puppies:
 2392
 dimethylbenzanthracene, skin, mouse: 2329
 embryonic kidney or lung cultures, mouse,
 review: 2128
 ethyl nitrosourea, brain, rat: 2283
 mechanism, review: 2116
 mouse leukemia viruses: 2352
- ubal-ligation sterilization, cervix cancer
 epidemiology, Puerto Rico: 2574
- IGLOSAN (See under Antitumor agents)
- ESTERONE
 effect on transplantable mammary tumors, mouse:
 2267
- ROLACTIN
 effect on transplantable mammary tumors,
 mouse: 2267
- ROSTATE
 methylcholanthrene-transformed cell lines,
 transplantation antigens, mouse: 2185
- ROSTATE NEOPLASMS
 epidemiology, relationship to leukemia, Japan:
 2601
- ROTEINS
 carcinogen binding
 mouse skin: 2221
 rat liver: 2242
 cytoplasmic, nitroquinoline oxide uptake,
Tetrahymena pyriformis: 2275
 liver, effect of *o*-aminoazotoluene, mouse:
 2234
 synthesis, avian myeloblastosis virus-infected
 blood cells, chick: 2377
- ROTOZOA
Tetrahymena pyriformis, nitroquinoline oxide
 uptake: 2275
- teridium aquilinum
 extracts, intestinal or bladder tumors, rat:
 2314
- 3-PYRAZOLIDINONE, 1-PHENYL-
 toxicity, rat or mouse: 2305
- PYRENE
 metabolism, mouse embryo cells: 2219
- PYRROLIZIDINE ALKALOIDS
 liver toxicity, rat: 2308
- QUINAZOLINE, 2-METHYLTRICYCLO-
 effect on skin histochemistry, mouse: 2271
- QUINAZOLINE, 3-METHYLTRICYCLO-
 skin tumors, mouse: 2271
- QUINOLINE COMPOUNDS
 DNA photosensitization: 2203
- RADIATION CARCINOGENESIS, EXPERIMENTAL
 cell growth kinetics, review: 2125, 2126, 2127
 endocrine tumors, rat: 2177
 lung, rat: 2176, 2171
 ovary, lung, liver and RES, mouse: 2178
 skin, mouse, review: 2124
 thyroid, rat: 2175, 2257, 2265
 review: 2132
- RADIATION CARCINOGENESIS, HUMAN
 children, prenatal irradiation, latent
 periods: 2169
 maxillary carcinoma, basal cell nevus syndrome
 (familial): 2163
 mechanism, review: 2131
 sunlight
 lip cancer, U.S., geographical variations:
 2530
 skin cancer, pathogenesis: 2161
 Sweden: 2529
 thorium, bile duct carcinoma: 2170, 2172
 thyroid cancer, epidemiology, New York
 (Rochester): 2173

RADIATION EFFECTS

- cellular DNA synthesis, Shope virus-infected rabbit cells: 2475
- goitrogenic capacity of thyroid, rat: 2174
- immunity, methylcholanthrene-induced sarcoma, mouse: 2196
- light, effect on Rous virus transformation, chick embryo cells: 2387
- liver cancer incidence, Japan (Hiroshima/Nagasaki): 2559
- mutagenesis, Rous sarcoma virus (Schmidt-Ruppin strain), chick embryo: 2381
- plastic implant tumor development, rat or dog: 2299
- short-wave irradiation of brain, effect on methylcholanthrene tumors, rat: 2192
- skin carcinogenesis by detergent additives, mouse: 2301

RADIATION LEUKEMOGENESIS, EXPERIMENTAL

- cell growth kinetics, thymus: 2164
- cell surface antigens, mouse: 2351
- effect of

- Gross leukemia virus, rat: 2355
- thymectomy, mouse: 2355
- thymic and RES tumors, mouse: 2178

RADIATION LEUKEMOGENESIS, HUMAN

- children, prenatal irradiation, latent periods: 2169
- chromosomes, Hiroshima: 2165
- Japan

- Hiroshima and Nagasaki: 2602, 2603
- occupational radiation exposure: 2166, 2167
- therapeutic radiation: 2166, 2167, 2168, 2604

- perinatal and congenital, twins, review: 2136
- Ph¹-positive chronic myeloid leukemia: 2635

RADIOACTIVE ISOTOPES AND ELEMENTS

- cerium hydroxide dust containing radon, lung tumors, rat: 2171
- ¹²⁵I or ¹³¹I, thyroid tumors, rat: 2132, 2175, 2257, 2265

- ³²P, therapeutic, effect on chromosomes, polycythemia vera: 2641

- ²³⁹Pu distribution, effect of oophorectomy, rat: 2299
- endocrine tumors, rat: 2177
- lung tumors, rat: 2176, 2177

- ⁹⁰Sr, leukemia, effect of thymectomy, mouse: 2355
- thorium, bile duct cancer, human: 2170, 2172

RECTUM NEOPLASMS

- epidemiology
- appendectomy, West Germany: 2587
- California (Los Angeles), ethnic groups: 2556
- Jamaica: 2557, 2622
- Tennessee (Nashville) ethnic groups: 2555

RESINS

- intermediates in acetone or phenol production, skin tumors and leukemia, animal: 2304

RESPIRATORY DISEASES

- bronchial epithelial cell abnormalities (smokers and other persons), classification: 2319
- bronchitis
- air pollution, data evaluation methods: 2537

RESPIRATORY DISEASES, (Contd.)

- bronchitis, (Contd.)
- epidemiology, Great Britain (including Scotland), air pollution and smoking: 2535, 2536

RETICULOENDOTHELIAL SYSTEM

- function, transplanted mammary tumor development, mouse: 2646

RETRORSINE

- toxicity, liver, monkey: 2298

SACCHARIN

- effect on g.i. tract, mouse: 2315

SALIVARY GLAND NEOPLASMS

- epidemiology, Sweden (Stockholm): 2584

SCAR TISSUE (See also under Injuries)

- bronchial scleroderma, malignant transformation, case and review: 2153
- esophagus, malignant transformation: 2159, 2160, 2669, 2670
- skin, malignant transformation: 2158, 2162, 2666

SEX CHROMOSOMES

- mosaicism (XX/XXY; Klinefelter's), with lung cancer, SV40 transformation of WBC and fibroblast cultures: 2456
- uterine carcinoma: 2661

SEX DIFFERENCES

- plastic implant tumors, mouse: 2300
- smoking-associated lung cancer
- California (San Diego): 2541
- Jews, Montreal or Pittsburgh: 2539, 2540

SHOPE FIBROMA VIRUS (See under Virus, pox)

SHOPE PAPILLOMA VIRUS (See under Virus, papova)

SIMAZINE (See s-Triazine, 2-chloro-3,6-bis-(ethylamino)-)

SKIN

- specific carcinogen-binding protein, analysis, mouse: 2221
- toxicity, benzfluoranthene or tribenzfluoranthene, mouse: 2237

SKIN CARCINOGENESIS

- amphibian, review: 2157
- benzpyrene, mouse: 2237
- coumarin compound (detergent additive), radiation effects, mouse: 2301
- dimethylbenzanthracene
- hamster cheek pouch: 2225, 2229, 2230
- loss of malignancy, mouse, review: 2157
- transplacental, mouse: 2329
- mammals, review: 2124, 2127, 2157
- medicinal wax (ozokerite ceresin), mouse: 2307
- methylcholanthrene, mouse: 2182, 2186, 2191, 2195, 2197
- 3-methyltricycloquinazoline, mouse: 2271
- pyrolytic resins intermediate in acetone or phenol production, mouse or rabbit: 2304
- radiation and croton oil phorbol esters, mouse: 2299
- role of intramitochondrial dense bodies, mouse: 2184
- s.c. tumors
- avian adenovirus (CELO), hamster: 2511

IN CARCINOGENESIS, (Contd.)

- carboxynitroquinoline oxide-transformed cells, hamster: 2274
- dimethylbenzanthracene, effect of estrogen or orchiectomy, rat: 2264
- effect of CNS-acting treatment, rat: 2192
- methylcholanthrene
 - host immunity, mouse: 2183, 2196
 - rat: 2190, 2193, 2194
- plastics
 - blood supply, rat, review: 2117
 - karyotype, strain and sex differences, mouse: 2300
 - plastics, radiation effects, rat or dog: 2299
- spontaneously transformed rat embryo cell cultures, karyotype: 2628
- surgical adhesives, strain differences, mouse: 2306
- soil extracts of low or high benzpyrene content, mouse: 2213
- stilbene derivatives (detergent additives), radiation effects, mouse: 2301
- sunlight, pathogenesis: 2161
- s-triazine compounds, mouse or rat: 2272

IN DISEASES

- von Recklinghausen's disease, relationship to neuroblastoma, child: 2656

IN NEOPLASMS

- calcifying Malherbe's epithelioma, malignant transformation, case: 2657
- epidemiology, sunlight: 2161, 2529
- familial basal cell nevus syndrome, radiation-induced maxillary cancer: 2163
- epidermodysplasia verruciformis transforming to carcinoma, verruca vulgaris virus particles, case: 2501
- melanoma, malignant transformation of epithelial nevus: 2671
- nevus sebaceous, risk of supervening malignant tumor: 2527
- papilloma, Atlantic eel (*Anguilla vulgaris*): 2667
- scar tissue: 2158, 2162, 2666
- Shope papilloma virus-induced, mitotic activity during keratinization, rabbit: 2473

DIUM CHLORIDE

- benzpyrene content, drying methods: 2210

IL

- benzpyrene content
 - airport area, USSR (Moscow): 2212
 - bioassay (mouse skin): 2213

RONOLACTONE

- effect on dimethylbenzanthracene mammary tumors, rat: 2227

EEN

- pathology, Rauscher viral leukemia, mouse: 2349

ERIGOMATOCYSTIN

- toxicity, liver, monkey: 2298

LBENE, N-HYDROXY-4-ACETYLAMINO-, ACETIC ACID ESTER

- mutagenesis, bacteria: 2239

LBENE DERIVATIVES

- detergent additives, skin tumors, radiation effects, mouse: 2301

MACH NEOPLASMS

- epidemiology

STOMACH NEOPLASMS, (Contd.)

epidemiology, (Contd.)

- appendectomy, West Germany: 2587
- Armenian SSR (Yakutsk): 2548
- geographical variations
- Japan (Osaka and Nara prefectures) 2546
- Utah: 2552
- Uzbekh SSR, ethnic groups: 2547
- Yugoslavia: 2549
- Kenya (western) and Tanzania (northwestern): 2520
- pernicious anemia, (Minneapolis): 2551
- Poland (Cracow or Warsaw): 2550, 2623
- relationship to leukemia, Japan: 2601
- Rumania, urban and rural: 2515

STRESS

- electrical injury, tumor stimulation, mechanism, rat: 2181
- noise, effect on methyltrimethylaminoazobenzene liver tumors, rat: 2180
- rotary motion, effect on methyltrimethylaminoazobenzene liver tumors, rat: 2179

SUCROSE

- effect on g.i. tract, mouse: 2315

SURGERY

- appendectomy
 - cancer risk, West Germany: 2587
 - or tonsillectomy, cancer risk, New York (Kings County): 2586
- SV40 (See under Virus, papova)

TEMPERATURE, BODY

- diurnal changes, normal and tumor-bearing rat: 2652

TEMPERATURE, LOW

- effect on virus development, Lucké renal adenocarcinoma, frog: 2492

TERATOGENESIS

- carcinogens, animal, review: 2129
- mathematical model, review: 2130

TESTIS NEOPLASMS

- embryonal carcinoma, serum α -fetoprotein, review: 2134
- epidemiology, Finland: 2578
- occurrence, possible genetic or viral influence, Mexican axolotl (*Ambystoma mexicanum*): 2650

TESTOSTERONE PROPIONATE

- effect on transplantable mammary tumors, mouse: 2267

THIOURACIL, 6-METHYL-

- effect on ¹³¹I thyroid carcinogenesis, rat: 2257

- hormone imbalance, effect on methylnitrosourea-induced brain tumors, rat: 2284

- thyroid tumors, effect of electrical injury, rat: 2181

THOROTRAST (See under Radioactive isotopes and elements)

THYMUS

- growth kinetics, radiation-induced leukemia, mouse: 2164
- thymectomy, effect on radiation leukemogenesis, mouse: 2355

THYMUS NEOPLASMS

SUBJECT INDEX

THYMUS NEOPLASMS, (Contd.)

dimethylbenzanthracene- or 6-mercaptapurine-
induced lymphomas, alkaline phosphatase,
mouse: 2389

induction

ethylnitrosourea, strain A mice: 2282

Moloney leukemia virus-transformed rat

thymus cells, rat: 2356

THYROID

goitrogenic capacity, radiation effects, rat:
2174

mouse strains with high or low ¹³¹I uptake:
2644

THYROID NEOPLASMS

benign or malignant, factors affecting malignancy, animal, review: 2119

epidemiology

radiation exposure, New York (Rochester):
2173

world, review: 2133

induction

¹²⁵I or ¹³¹I, rat: 2175

¹³¹I, effect of methylthiouracil, rat: 2257

and low-iodine diet, effect of hypophysectomy, rat: 2265

methylthiouracil and hemithyroidectomy,

effect of electrical injury, rat: 2181

transplanted iodine-deficient goiter, rat:
2266, 2629

medullary carcinoma with amyloid stroma,

epidemiology, Switzerland (Lausanne): 2585

radiation-induced, rat, review: 2132

TOBACCO

chewing, oral and pharyngeal cancer, India
(Madhya Pradesh), ethnic groups: 2531

hybrid strain (*Nicotiana glauca* x *N.*

langsdorffii), tumor induction, tobacco

smoke condensate: 2322

powdered, lung or liver tumors and leukemia,
mouse: 2318

snuff, nasal cavity tumors, historical review:
2115

TOBACCO SMOKE

analysis, nitrogen compounds, review: 2156

ciliostasis, effect of metaproterenol, rabbit
trachea *in vitro*: 2323

toxicity

lung, measurement method, mouse: 2317

rabbit trachea *in vitro*: 2323

tumor induction, hybrid tobacco plant: 2322

TOBACCO SMOKING

bladder cancer, U.S.: 2544

brain tumors, Minnesota: 2580

bronchial cancer, East Germany: 2543

epithelial cell abnormalities, classification:
2319

bronchitis, Great Britain (including Scotland):
2535, 2536

lip cancer, U.S.: 2530

lung cancer

California (San Diego), sex difference:
2541

East Germany: 2543

Japan (cities near Osaka): 2538

Jews, sex difference, Montreal or Pittsburgh:
2539, 2540

TOBACCO SMOKING, (Contd.)

lung cancer, (Contd.)

Scotland, urban and rural: 2536

South Africa, ethnic groups: 2542

o-TOLIDINE

poisoning, mechanism, rat: 2232

m-TOLUENEDIAMINE

liver tumors, effect of other carcinogens,
rat: 2235

TONSILLECTOMY (See under Surgery)

TOXICITY

aflatoxin, liver, monkey: 2298

benzfluoranthene or tribenzfluoranthene,
mouse: 2237

benzidine and related compounds, rat: 2232

benzpyrene or dimethylbenzanthracene,
mammalian fibroblasts, species difference:
2202

beryllium and beryllium-containing rocket
exhaust products, rodent: 2312

evaluation methods, mathematical model, review:
2130

photographic emulsion component or developing
agent, rat or mouse: 2305

pyrrolizidine alkaloid, liver, rat: 2308

retrorsine, liver, monkey: 2298

sterigmatocystin, liver, monkey: 2298

tobacco smoke

lung, mouse, measurement method: 2317

rabbit trachea *in vitro*: 2323

TRACHEA

tobacco smoke-induced ciliostasis, effect
of metaproterenol *in vitro*, rabbit: 2323

TRACHEA NEOPLASMS

cell growth kinetics, measurement method: 2614

TRANSPLACENTAL CARCINOGENESIS (See under Pregnancy)

TRAUMA (See Injuries)

TRIAZENE, PHENYLDIMETHYL-

brain tumors, enzymes, rat: 2269, 2270

s-TRIAZINE, 2-CHLORO-3,6-BIS(ETHYLAMINO)-

g.i. and skin tumors, mouse or rat: 2272

s-TRIAZINE-2,4,6-TRIOL

liver or skin tumors, mouse or rat: 2272

URBANIZATION (See under Environmental factors)

UREA, 3-(p-CHLOROPHENYL)-1,1-DIMETHYL-

effect on glycolysis, rat liver: 2263

URETHAN

cytotoxicity, embryonic mouse lung cultures:
2290

leukemia

effect of leukemia virus, mouse: 2288

partial hepatectomy, mouse: 2286

liver tumors

effect of leukemia virus, mouse: 2288

partial hepatectomy, mouse: 2286

lung tumors

effect of influenza virus, mouse: 2291

leukemia virus, mouse: 2288

partial hepatectomy, mouse: 2286

relation to postnatal cellular proliferation,
mouse or hamster: 2287

metabolism, effect of partial hepatectomy,
mouse: 2285

metabolites, mutagenesis, *Drosophila*: 2289

toxicity, hamster (*Phodopus sungorus*): 2642

URETHAN, N-HYDROXY-
cytotoxicity, embryonic mouse lung cultures: 2290

UROKINASE
effect on transplanted tumors, mouse: 2302

UTERUS NEOPLASMS (See Corpus uteri neoplasms)

VAGINA NEOPLASMS
artificial vagina formed after surgery for cervical carcinoma, case: 2658

VERRUCA VULGARIS VIRUS (See under Virus, pox)

VINBLASTINE (See under Antitumor agents)

VIRAL CARCINOGENESIS
Moloney sarcoma virus, chicks and mammals: 2365
possible, testicular tumors, Mexican axolotl (*Ambystoma mexicanum*): 2650
review: 2126, 2140, 2142, 2143
Rous sarcoma virus
(Carr-Zilber strain), mouse: 2371
(Schmidt-Ruppin strain) or leukemic human WBC, amphibia and reptiles: 2383

VIRUS
Cocal arbovirus
effect on Friend leukemia virus-induced splenomegaly, mouse: 2337
cytoplasmic
amphibian tumors (frogs and newts): 2497
Lucké frog kidney tumors: 2495
and nuclear, Burkitt lymphoma biopsy specimens: 2478
DNA-containing
effect on Shope fibroma virus, rabbit cells: 2476
effect of aflatoxins, review: 2121
exposure
liver cancer risk, international: 2561
perinatal and congenital leukemia, twins, review: 2136
frog virus 3
effect on cellular DNA and RNA, human tumor (KB) cells: 2498
hepatitis
Australia antigen, leukemia or Hodgkin's disease: 2591
influenza
effect on urethan lung tumors, mouse: 2291
paramyxo-like
effect on SV40 rescue, transformed hamster cells: 2508
particles resembling
plasmacytoma of frog with Lucké tumor transplant: 2496
polio
infectivity, SV40-transformed human cells: 2454
PR-8 myxovirus
immunization, effect on oncogenicity of lung cultures, hamster: 2462
reovirus Type 3
Burkitt lymphoma, review: 2138
RNA-containing
effect on Shope fibroma virus, rabbit cells: 2476

VIRUS, (Contd.)
Sendai
inactivated, effect on chick fibroblast-hamster Rous sarcoma heterokaryons and antigens: 2384
infection, immunosuppression, SV40 or adenovirus-16, hamster: 2418
UV-irradiated, SV40 rescue, transformed cells: 2435
"slow" virus infection, Hodgkin's disease and multiple sclerosis, review: 2139
UV-HVJ
fusion of Ehrlich carcinoma and azaguanine-resistant L cells, properties of hybrid cells: 2499

VIRUS, ADENO-
associated virus Types 1, 2 and 3
serum antibodies, human cancer: 2589
bovine Type 3
isolation and properties of non-oncogenic variant, hamster: 2403
serum antibodies to T antigen, human cancer: 2588
WB-PS variant, new antigens, infected hog kidney cells or hamsters: 2402
canine hepatitis
serum antibodies to T antigen, human cancer: 2588
CELO (avian)
hamster tumors, properties and pathology: 2416
Petak or Phelps strain, hamster tumor cells, virus-specific tumor antigen: 2415
s.c. sarcoma or hepatoma (hamster) and T antigens (infected chick cells): 2511
human, subgroups A, B and C
serum antibodies to T antigens, human cancer: 2588
rodent tumors or transformed cells, nucleic acid homology studies, review: 2145
SA-7 (simian)
brain tumors, hamster: 2414
effect on SV40-transformed monkey kidney cells: 2438
hamster tumors, strain difference: 2412
SA7(C8) simian
specific tumor immunity, hamster: 2413
simian, subgroups I, II and III
serum antibodies to T antigen, human cancer: 2588
SV30 (simian)
infected monkey kidney cells, ultrastructure: 2417
Type 2
effect on SV40 infection or transformation, monkey kidney cells: 2400, 2438
SV40 hybrids, properties of viruses and transformed cells: 2420, 2423, 2424, 2425, 2426
Type 3
cross-reacting tumor-specific transplantation antigens, mouse tumors: 2401
Type 5
effect on nuclear ultrastructure, human tumor cells: 2404

VIRUS, ADENO-, (Contd.)

Type 7

- effect on SV40-transformed monkey kidney cells: 2438
- SV40 hybrids, properties: 2420, 2470
- SV40(PARA) hybrids, properties of virus and transformed cells: 2419, 2421, 2422
- transformation, cell growth kinetics, monkey kidney cells: 2470

Type 12

- effect on DNA, hamster cells: 2512
- SV40-transformed monkey kidney cells: 2438
- hamster tumors: 2405, 2407, 2409, 2412
- cellular antigens: 2407, 2408, 2411
- infected human cells, antigens: 2408, 2411
- mouse tumors, antigens: 2401, 2411
- serum antibodies, monkey: 2406
- SV40 as helper, monkey kidney cells: 2445
- SV40 hybrid, transformed hamster cells, properties: 2423, 2424
- transformation, monkey kidney cells: 2410

Type 14

- mouse tumors, cross-reacting tumor-specific transplantation antigens: 2401

Type 16

- effect on SV40 tumors, hamster: 2429
- immunosuppression, Sendai virus-infected hamster: 2418

VIRUS, HERPES

herpes simplex

- effect on Shope fibroma virus, rabbit cells: 2476
- genital or lip cancer, human, review: 2147
- rabbit antisera, comparison with Epstein-Barr virus antisera: 2480

Type 1 or 2

- effect on SV40-transformed monkey kidney cells: 2438
- serum antibodies, cervix cancer, Georgia (Atlanta): 2576

VIRUS, HERPES-TYPE

Epstein-Barr (human)

- common antigen with Lucké virus: 2489
- DNA homology, virus-free Burkitt lymphoma cell line: 2479
- leukemia and lymphoma, human, review: 2138, 2146, 2148
- morphology, Burkitt lymphoma biopsy specimens: 2478
- rabbit antisera, comparison with herpes simplex antisera: 2480
- serum antibodies
 - acute leukemia with infectious mononucleosis, case: 2482
 - early viral antigens, human: 2481
 - mammals and frogs: 2492

leukovirus (human)

- human WBC cell lines (normal, malignant or non-malignant diseases): 2631

Lucké (frog)

- associated cytoplasmic viral particles: 2495
- attempted horizontal and vertical transmission: 2493
- common antigen with Epstein-Barr virus: 2489

VIRUS, HERPES TYPE, (Contd.)

Lucké (frog), (Contd.)

- effect of temperature, tumor transplants: 2492
- epidemiology of virus-positive tumors, Minnesota, North Dakota and Louisiana, seasonal changes: 2494
- latent period, kidney tumors, frog: 2490
- Marek's disease (chicken)
 - Biken A, B or C strain, nuclear and cytoplasmic inclusions, duck embryo cells: 2488
 - effect of bromodeoxyuridine, chick or duck embryo cells: 2487
- JM strain
 - cell-free transmission and replication, chick: 2486
 - cellular antigens, chick kidney cells: 2483
 - tissue antigens, infected or tumor-bearing chickens: 2484
- morphogenesis and antigen formation, chick or duck embryo cells: 2485
- review: 2149, 2150
- RPL39 strain, tissue antigens, infected or tumor-bearing chickens: 2484

VIRUS, HYBRID

- adenovirus 2-SV40
 - properties of viruses and transformed cells: 2420, 2423, 2424, 2425, 2426
- adenovirus 7-SV40
 - properties: 2420, 2470
- adenovirus 7-SV40 (PARA)
 - properties: 2419, 2421, 2422
- adenovirus 12-SV40
 - transformed hamster cells, properties: 2423, 2424

VIRUS, LEUKEMIA/LYMPHOMA

AKR (mouse)

- immune virolysis: 2335

avian leukovirus

- effect on infectious RSV(0) synthesis, chick embryo cells: 2385

avian myeloblastosis

- viral RNA and complementary cellular DNA leukemic chickens: 2378

BAI strain A (avian myeloblastosis)

- RNA and protein synthesis, infected blood cells, chick: 2377

bovine leukosis

- leukemia epidemiology, Europe, review: 2135
- 334C (mouse)
 - horizontal transmission: 2352

cat

- Type C particles, in vitro detection method: 2390

Friend (mouse)

- Axelrad strain (polycythemia- and splenic focus-inducing), immunosuppression, mouse: 2338
- effect of interferon or interferon-stimulating antibiotic, mouse: 2346
- effect on
 - transplanted rat tumors, mouse: 2344
 - rat: 2345
- F-S or F-B strains, identification of gene governing splenic focus formation: 2336

SUBJECT INDEX

VIRUS, LEUKEMIA/LYMPHOMA, (Contd.)

Friend (mouse), (Contd.)

- genetic susceptibility, mouse strains: 2539, 2340
- horizontal transmission: 2352
- immunosuppression, mouse: 2338
- infection, strain differences and host immunity, mouse: 2343
- interference, Cocal arbovirus, mouse: 2337
- liver or spleen tetrahydrofolate dehydrogenase, mouse: 2350
- replication, transplanted mouse tumor: 2342
- transplantable rat tumor (WFT-2N), cellular immunity: 2341

Graffi (mouse)

- pathology, tissue cultures: 2357

Gross (mouse)

- effect on radiation leukemogenesis, rat: 2355
- surface antigens: 2351, 2505

human

- review: 2146
- transmission, mouse: 2502
- virus-like particles, primates with transmitted human leukemic cells or filtered blood: 2503

L₂C (guinea pig)

- pathogenicity, Strain 2 or hybrid guinea pig: 2633, 2634

Mazurenko (mouse)

- tissue antigens, mouse: 2354

Moloney (mouse)

- defective and competent, replication, mouse cells: 2359
- infected and tumor-inducing rat cell lines: 2356
- liver or spleen tetrahydrofolate dehydrogenase, mouse: 2350
- surface antigens: 2351

mouse

- classification method: 2353
 - intracisternal and Type C particles, antibody-producing cells, autoimmune NZB mice: 2332
 - isolation (spontaneous leukemia of C58 mice) and effect on CNS, age factors, mouse: 2331
 - leukemia-sarcoma complex
 - focus formation, mathematical model: 2333
 - sensitivity assay method: 2358
 - 6-mercaptopurine-induced lymphoma, tumor alkaline phosphatase: 2389
 - myeloid chloroleukemia, effect on urethan carcinogenesis, mouse: 2288
 - possible activation, mammary tumor virus, mouse: 2397
 - serum group-specific viral antibodies
 - high- or low-leukemia mouse strains: 2348
 - mice or rats with methylcholanthrene-induced or viral sarcomas: 2348
- RadLV radiation leukemia virus (mouse)
- sarcoma virus complex, focus formation, mouse embryo cells: 2334

VIRUS, LEUKEMIA/LYMPHOMA, (Contd.)

Rauscher (mouse)

- horizontal transmission: 2352
- immunosuppression, NZB mice: 2347
- liver or spleen tetrahydrofolate dehydrogenase, mouse: 2350
- lymph node pathology, mouse: 2349
- surface antigens: 2351

T/S (mouse)

- isolation (I_b line leukemia) and effect on CNS, age factors, mouse: 2331

VIRUS, MAMMARY TUMOR

Bittner (mouse)

- effect on growth rate, mouse kidney cells: 2394
- morphogenesis, spontaneous C3H mammary tumors: 2393

mouse

- centrifugation patterns: 2397, 2398
- cross-reactivity with embryonic antigens, mouse: 2396
- effect on skin, intramitochondrial dense bodies: 2184
- high-tumor PBA strain: 2643
- possible leukemia virus activation, mouse: 2397
- spleen cultures of infected mice, virus-associated surface antigens: 2399
- transfer RNA-methylating enzymes of tumor cells: 2647
- Type A and B particles, transplantable mammary tumor (Adenocarcinoma #755), mouse: 2395

VIRUS, PAPOVA (papilloma-polyoma-vacuolating)

equine papilloma

- ultrastructure: 2472

polyoma

- carrier population, mouse cells: 2464
- DNA, effect on cellular genetics, mammalian cells, review: 2144
- effect on DNA, mouse embryo cells: 2467
- immunization, effect on oncogenicity of lung cultures, hamster: 2462
- infected mouse cells, light satellite-band DNA: 2463
- large- or small-plaque strains, DNA ultrastructure: 2465
- mouse tumors, serum antibodies to polyoma tumor-specific surface antigens: 2457
- particles resembling, progressive multifocal leukoencephalopathy and chronic leukemia, case: 2471
- rat tumors, leukemia virus group-specific antigen: 2348
- RBC receptors, human: 2466
- strain 3049/P1B2, capsid antigen, infected mouse cells: 2458
- thermosensitive mutant (Ts-a), transformed cells, properties: 2468, 2469
- Toronto strain (small-plaque)
 - effect on mouse-hamster somatic hybrid cells: 2461
 - transformation, hamster brain cells: 2460
 - transformation, cell growth kinetics, hamster cells: 2470

VIRUS, PAPOVA, (Contd.)

(papilloma-polyoma vacuolating), polyoma, (contd.)

transformed cells

hamster, lysosomes: 2459

mouse, tumor-specific transplantation antigens: 2432

Shope papilloma

mitotic activity during keratinization, rabbit tumor: 2473

SV40

adenovirus-2 hybrids, properties of viruses and transformed cells: 2420, 2423, 2424, 2425, 2426

adenovirus-7 hybrids, properties: 2420, 2470

adenovirus-12 hybrids, transformed cells, properties: 2423, 2424

defective (PARA), adenovirus-7 hybrids, properties: 2419, 2421, 2422

DNA

cleavage, bacterial endonuclease: 2506

replication, monkey kidney cells: 2437, 2439, 2447

effect on adenovirus-2 infection, monkey cells: 2400

hamster tumors, effect of immunization by irradiated SV40-transformed cells: 2431

helper for adenovirus-12, monkey kidney cells: 2445

immunosuppression, Sendai virus-infected hamster: 2418

infected cells, animal or human: 2427, 2441, 2442, 2443, 2444, 2449, 2509

infection, monkey: 2440

pseudovirions, detection and properties, monkey kidney cells: 2447

rescue: 2435, 2452, 2508

serum antibodies, rabbit: 2428

strain A426

hamster tumors, effect of adenovirus-16: 2429

T antigen, mammalian cells, species differences: 2450

transformation

human cells: 2434, 2451, 2454, 2470

monkey cells: 2451, 2470

mouse cells: 2358, 2470

species difference, rodent cells: 2430

XX/XXY mosaic cells from pt. with Klinefelter's syndrome and lung cancer: 2456

transformed cells

antigenicity, cell culture or hamster: 2431, 2507

hamster tumors, surface antigen(s): 2448

human amnion, properties: 2453, 2455, 2510

monkey kidney, susceptibility to superinfection: 2438, 2446

mouse, properties: 2432, 2433, 2436, 2448

tumor induction (hamster) and cellular immunity (rat or mouse): 2433

VIRUS, POX

myxoma or vaccinia

VIRUS, POX, (Contd.)

myxoma or vaccinia, (Contd.)

effect on Shope fibroma virus, rabbit cells: 2476

Shope fibroma (rabbit)

cellular immunity, measurement, infected rabbit cells: 2474

Patuxent strain

cellular DNA, effect on radiation or contact inhibition, rabbit cells: 2475

effect of other viruses, rabbit cells: 2476

verruca vulgaris (human)

epidermodysplasia verruciformis with malignant transformation, case: 2501

Yaba histiocytoma (monkey)

adaptation and growth kinetics, monkey kidney cells: 2477

VIRUS SARCOMA

cat

S-T fibrosarcoma, tumor pathology and ultrastructure, kitten: 2391

Type C particles, S-T fibrosarcoma virus-induced tumors, kitten: 2391

cat fibrosarcoma

transmission, marmoset: 2504

transplacental, cat or dog: 2392

Claude's CTV-10 (chicken)

virus titer and effect of amputation, chicken: 2379

Harvey (mouse)

effect on sugar transport, transformed or infected cells: 2360

hamster tumors, ultrastructure: 2362, 2364

rat osteosarcoma, ultrastructure: 2364

transformation, mouse embryo cells: 2361

tumor pathology, mouse: 2363

Moloney (mouse)

defective, replication, mouse cells: 2359

rescue, hamster tumor: 2369

immunosuppression, mouse: 2370

transformation, mouse cells: 2361, 2366

tumor pathology

chick or rodent: 2365

hamster: 2362, 2364, 2365

mouse: 2363, 2365, 2367

rat: 2364, 2365, 2368

mouse

leukemia-sarcoma complex

focus formation, mathematical model: 2333

sensitivity assay method: 2358

pseudotype of radiation leukemia virus, leukemia virus complex, focus formation, mouse embryo cells: 2334

transformed cells, effect of serum growth factor: 2436

Rous (chicken)

APL-22 strain

serum antibodies, domestic and wild birds, USSR: 2382

Bryan strain

resistance, chick embryo cells: 2376

serum antibodies, domestic and wild birds, USSR: 2382

transformation, effect of antimetabolite or light, chick embryo cells: 2387

VIRUS, SARCOMA, (Contd.)

- Rous (chicken), (Contd.)
- Bryan strain, (Contd.)
 - transformed hamster cells, virus-specific antigens: 2374
- Carr-Zilber strain
 - mouse tumors, mouse variant virus: 2372
 - pathology: 2371
 - serum antibodies, domestic and wild birds, USSR: 2382
- effect on DNA and RNA, infected or transformed chick embryo cells: 2386
- Engelbreth-Holm strain
 - serum antibodies, domestic and wild birds, USSR: 2382
- hamster tumors: 2375, 2384
- mouse or rat tumors, leukemia virus group-specific antigen: 2348
- properties of tumor cell DNA, chick: 2648
- RSV(0)
 - cell-associated factor required for synthesis of infectious virus, chick embryo cells: 2385
- Schmidt-Ruppin strain
 - mouse variants: 2372
 - mutagenesis, radiation, chick embryo: 2381

VIRUS, SARCOMA, (Contd.)

- rat tumors, pathology and strain differences: 2373
- RNA-dependent DNA polymerase in virions: 2388
- serum antibodies, domestic and wild birds, USSR: 2382
- tumor induction, amphibia and reptiles: 2383
- strain D
 - replication, chick embryo cells: 2380

WATER POLLUTION

- benzpyrene, review: 2116

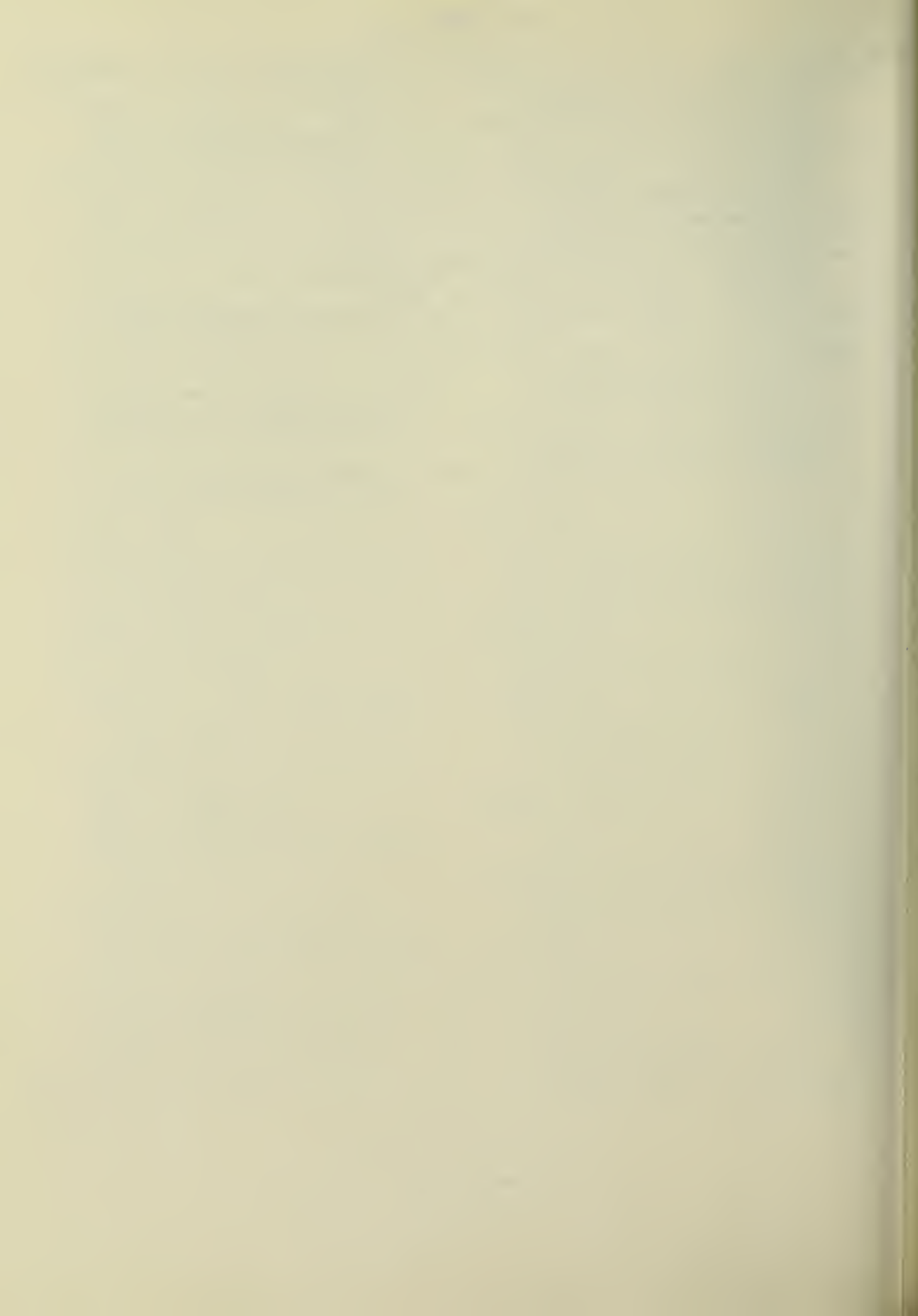
WAX, MEDICINAL

- ozokerite ceresin (from USSR), carcinogen content and skin carcinogenesis (mouse): 2307

WOOD

- smoke
 - drying method, effect on benzpyrene content of prunes: 2215
 - effect on benzpyrene content of fish: 2209

YABA VIRUS (See under Virus, pox)









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Subject-Author Index

Vol. 8

CARCINOGENESIS
ABSTRACTS

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- Aaronson, S. A. 442,812,851,
1293,1752,2358
Abdel-Tawab, G. A. 1099
Abdullakhodzhaeva, M. S. 1819
Abe, T. 556
Abelev, G. I. 2348
Abell, M. R. 2331
Abelson, H. T. 1620
Acheson, E. D. 1658
Achord, J. L. 962
Ackerman, E. 940
Ackman, P. 1412
Adamiker, D. 211
Adams, C. 2474
Adams, D. H. 103
Adams, R. A. 1709, 2470
Adelberg, M. 2053
Adenis, L. 238,395,1082,1083
Aderca, I. 2020,2449
Adler, D. 137
Adler, S. P. 2506
Adrian, R. W. 1840
Adzhigitov, F. I. 2406,2410
Agarwal, M. K. 1538,2243
Agarwal, S. 2531
Ageenko, A. I. 2413
Agresti, A. 1679
Ahearn, M. J. 1582,1966
Ahl, R. 752
Ahlström, C. G. 1238
Ahmed, N. 1369
Ahuja, E. M. 2571
Aikawa, S. 2012
Ajuria, E. 441,1576,1982
Akamatsu, Y. 1539
Akasu, F. 967
Akimova, R. N. 726
Albert, R. E. 1038,1560
Albrecht, C. 1141
Alcini, E. 390
Aldenderfer, P. 151
Aleksandrov, V. A. 1876
Aleksandrowicz, J. 916,1391,
1392,2135
Alexandrescu, M. 306
Alexandrov, K. 380,1525
Alexandrov, S. N. 1744
Alexandrov, V. A. 713
Al-Falluji, M. M. 864,2058
Alford, T. C. 838,2003,2405
Alfred, L. J. 36
Algard, F. T. 1130,1833
Allcroft, R. 2294
Allen, A. 2319
Allen, J. L. 437
Allen, J. R. 2308
Allgaier, C. 789
Alli, A. F. 1667
Allison, A. C. 281,411,875,
876
Aloni, Y. 1280
Alonso, A. 1869
Alpert, E. 1913
Alpert, M. E. 1374
Alquati, P. 390
Al-Saadi, A. A. 2629
Altaner, C. 1963
Altenbrunn, H.-J. 169
Althoff, J. 1537
Altman, R. F. A. 198,1064
Altmann, H. 211
Al'tshtein, A. D. 2022,2413,
2430,2433,2450
Alvares, A. P. 1091
Alvarez, Y. 1294
Amaral, L. 1192
Amaral-Mendes, J. J. 1039
Ambrose, E. J. 147,148
Ambrose, K. R. 845
Ambrosioni, J. C. 1632
Ambrus, J. L. 1637
Ames, R. P. 822,1297,1567,
1621
Ames, W. R. 23
Amiel, J. L. 1575
Amirante, E. 1702
Amlacher, E. 1805
Amsel, S. 156
Anderer, F. A. 435
Anders, F. 334
Andersen, R. A. 2322
Anderson, C. K. 922
Anderson, D. E. 2456
Anderson, D. L. 895
Anderson, J. 124,833,2511
Anderson, N. G. 845
Anderson, T. J. 2281
Andervont, H. B. 1599
Andrea, J. 1779
Andreoli, A. 1970
Andresen, W. F. 346
Andrianov, L. A. 1815
Angervall, L. 1123,2545
Angulo-Hernández, O. 1362
Ankerst, J. 121,2401
Ansfield, F. J. 1548
Anthony, J. J. 1909
Antonov, A. M. 2304
Aoki, K. 127
Aoki, T. 873,1262,2351
Aoyama, Y. 304
Aposhian, H. V. 2060
Appelgren, K. L. 974
Arachi, H. 2546
Araki, F. 1756
Araki, M. 432,616,1165,
1477
Archer, F. L. 938
Arcos, J. C. 191,199,1160
Argano, S. A. P. 1163
Argus, M. F. 191,199,1160
Arias, I. M. 1927
Arkhangel'skii, A. V. 2304
Armin, K. 2092
Armstrong, W. F. 2266
Arnaud, A. 1482
Arnaud, C. D. 2651
Arnott, S. J. 1045
Arnstein, P. 2392
Arquint, A. 2672
Arrhenius, E. 2240,2241
Arseculeratne, S. N. 670,1109
Asch, B. B. 2416
Ashkenazi, A. 2431
Ashley, D. J. B. 896,904,1660,1661,
2085,2086,2558
Ashley, L. M. 666
Ashmeade-Dyer, A. 884
Asman, H. B. 1332
Assal, N. R. 1353,1648
Athanasius, P. 2371
Atkin, N. B. 342
Atoynatan, T. 1276
Attridge, J. T. 1998
Auerbach, H. 1543,1753,2124,2299
Auerbach, O. 178
Auersperg, N. 141,142
Auger, C. 1093
Augl, C. 1959
Aungst, C. W. 1405
Aurelian, L. 2043
Avrameas, S. 849
Avtsyn, A. P. 2478
Awa, A. A. 1757
Axelrod, D. 501,2032
Axelsson, U. 2471
Aya, T. 317
Ayres, J. C. 1104,1105
Azami, M. A. 1536
Baba, S. 739,743
Baba, T. 1874
Bababunmi, E. A. 1107
Babakova, S. V. 2413
Bacigalupo, G. 2228
Bader, A. V. 809
Bader, J. P. 1944
Baerwald, R. J. 625
Bagby, S. P. 1622
Ba Giao, N. 206
Bahr, G. F. 341
Baikie, A. G. 1015
Bailar, J. C. 2094
Bailey, P. C. 2643
Baingana, N. 878
Bajtai, A. 1043
Bajwa, G. S. 1461
Baker, L. A. 265
Baker, M. C. 342
Baker, M. S. 36
Baker, R. S. U. 810
Bakke, O. M. 1489
Balasubramaniam, K. 670,1109
Balduzzi, P. 2387,2464
Baldwin, R. W. 203,245,2271
Balenko, N. V. 1793
Ball, J. K. 377,614
Balli, L. 990
Ballini-Kerr, I. 198
Balner, H. 391

Balslev, I. 898
 Baltimore, D. 1583
 Baluda, M. A. 2377,2378
 Bandunatha, C. H. S. R.
 1109
 Bandy, D. 365
 Banerjee, M. R. 292,1623
 Banfield, W. G. 555
 Banks, K. W. 722
 Banua, M. 965
 Banasch, P. 1884
 Banua, B. C. 1195
 Bara, N. 1568
 Barbanti-Brodano, G. 2441
 Barber, H. R. K. 557
 Barbieri, D. 1734
 Barbosa, O. 329
 Barcellona, P. S. 1463
 Bard, D. S. 43
 Barker, B. E. 977
 Arkhudarov, R. M. 1453
 Barnwell, E. B. 1623
 Barnes, C. A. 1031,1033
 Barroche, C. 626
 Barou, J. 646
 Barou, S. 444,461,843,
 1303
 Barr, L. M. 104
 Barrett, C. P. 1981
 Barwick, S. 868
 Barrow, N. A. 53
 Barry, E. J. 3,1540,2242
 Barzski, G. 149,1734
 Barson, A. J. 1346
 Barth, R. F. 131
 Bartko, D. 1738
 Bartlett, K. D. 599,2218
 Bartlett, G. L. 1541,
 1841
 Bartus, B. 61,1845
 Barzga, R. 1694
 Barzillo, C. 2461,2465
 Barzkar, J. F. 2390
 Barzker, J. F. 1965
 Barzur, P. K. 1177,1178
 Barzssir, O. 1107,1114
 Barztaillon, G. 466
 Barztes, B. 1307
 Barztes, R. R. 31,46,2223
 Barzteson, E. M. 2533
 Barzther, R. 110,803,
 1956,2648
 Barzttifora, H. A. 1849
 Barzuer, H. 789,1952,
 1954
 Barzuer, L. 1916
 Barzuke, J. 157
 Barzum, S. G. 2420
 Barzvetta, L. A. 1461
 Barzkendale, W. 832
 Barzsch, D. J. 1176
 Barzard, D. 779,1994
 Barzard, J. W. 778,779,
 1577,1994
 Barzardsley, R. E. 2500
 Barzaudreau, G. S. 1230

Bebawi, G. M. 1890
 Becker, J. 1120
 Becker, K. L. 1400
 Becker, Y. 831
 Bednarzewski, J. 359
 Behbehani, A. M. 868
 Beierwaltes, W. H. 2629
 Belamaric, J. 1382
 Belitskii, G. A. 2202,2219
 Bell, J. R. 690
 Belloncik, S. 516
 Belman, S. 4
 Beltran, G. 350
 Bem, J. 1818
 Ben, T. 85
 Ben-Bassat, H. 2427
 Bendall, R. 403
 Bender, E. 488
 Bendich, A. 1006
 Bendová, H. 2207
 Benedetti, E. L. 1845
 Benedict, W. F. 1010
 Benemanskii, V. V. 2280
 Bengge, M. C. 1479
 Bengtsson, U. 1123,2545
 Bennett, B. 415
 Bennett, J. E. 1331
 Bennett, M. 2338
 Benninghoff, D. L. 1036
 Ben-Porath, M. 2175
 Benso, L. 1605
 Bensted, J. P. M. 1464
 Bentley, J. P. 1466
 Bentvelzen, P. A. J. 115,481,
 818,1870,2399
 Benyesh-Melnick, M. 450,
 1616,2061
 Ber, A. 1832
 Berardet, M. 1575
 Berce, N. A. 1910
 Berdal, P. 1339
 Berebbi, M. 497
 Berenblum, I. 58,1023
 Berg, J. W. 1359,1665,
 2556
 Berg, P. 2469
 Berge, T. 1664,2583
 Berger, B. W. 2162
 Berger, R. 1733
 Bergol'ts, V. M. 578
 Bergs, M. 759,1598
 Bergs, V. V. 101,759,
 1598
 Berlie, J. 328
 Berman, L. D. 108,281,
 2423
 Bern, H. A. 116
 Bernard, C. 1624
 Bernard, J. 2594
 Bernard, P. 368
 Berndt, H. 2080,2587
 Bernelli-Zazzera, A. 2262
 Bernhard, W. 849
 Berry, C. L. 2105
 Berry, G. 183,1340
 Bersi, M. 954

Bertalanffy, F. D. 920
 Bertone, C. 519
 Beskrovnyi, A. M. 2226
 Beuving, L. J. 708,709
 Bhansali, S. K. 1448
 Bharadwaj, V. P. 695
 Bhargava, M. K. 1383
 Bhargava, S. K. 1383
 Bhide, S. V. 621,660
 Bianchi, L. 1057
 Biancificori, C. 1498,1500
 Biava, C. G. 573
 Bielschowsky, M. 1712
 Bierwolf, D. 1735
 Biggs, P. M. 1950
 Bigner, D. D. 797,1240
 Biliczki, F. 1654
 Bill, A. H., Jr. 1685
 Billheimer, F. E. 2439
 Bingham, E. 1087,2301
 Biquard, J.-M. 269
 Birbeck, M. S. C. 1103
 Bird, C. C. 1807
 Bird, E. S. 704
 Birg, F. 1273
 Biriulina, T. I. 278,2373
 Biscatti, G. 1702
 Bischoff, F. 999,1544,1936
 Biserte, G. 486,2404
 Bishop, D. 1098
 Biswal, N. 450
 Bixler, D. 1331
 Björklund, B. 751
 Bjørro, K. 1128
 Black, P. H. 1287,1324,2024,
 2423,2424
 Blackham, E. 1586
 Blackstein, M. E. 861
 Blackwell, R. 1101
 Blair, P. B. 1595,1627,2396,
 2398
 Blakeslee, J., Jr. 1643
 Blanchard, J. 1211
 Blankenburg, H. 2090
 Bleiberg, M. J. 2323
 Blizzard, R. M. 2106
 Bloch, D. A. 931
 Bloch, M. 2175
 Bloom, A. D. 1757
 Bloom, B. R. 415
 Blumberg, B. S. 2591
 Blume, R. S. 1407
 Blumenshine, J. A. 2312
 Blumenson, L. E. 2100,2613
 Blunck, J. M. 651,1893
 Bobrina, K. G. 2547
 Bock, F. G. 1542,1803,2205
 Bockman, D. E. 76
 Boeryd, B. 622,1469
 Bogden, A. E. 1990
 Boger, E. 1214
 Böhme, P. E. 1360
 Boiron, M. 805,807,1246,
 1624
 Boisseau, M. 1762
 Bolande, R. P. 2656

- Bolano, C. R. 868
 Bole, G. G. 2639
 Bolognese, R. J. 907
 Bolognesi, D. P. 779
 Bonakdarpour, A. 1875
 Bonar, R. A. 1577
 Bond, H. E. 478
 Bonmassar, A. 1993
 Bonmassar, E. 1993
 Bonneau, H. 496,497,856
 862,1273
 Bonser, G. M. 7
 Boone, C. W. 2645
 Booth, A. N. 365
 Bopp, W. J. 756,2112
 Boquoi, E. 1901
 Borek, C. 2111
 Borella, L. 1219,1318
 Borenfreund, E. 1006
 Borisiuk, Iu. P. 1768,
 2215,2307
 Borisov, B. K. 1453
 Borland, R. 331
 Borneff, J. 1785
 Börner, P. 195
 Borsos, R. 1578
 Borsos, T. 654,655,
 656,2633
 Borum, K. 1077
 Bosch, A. 2574
 Boschetti, E. 1229
 Bösenberg, H. 663,664
 Bosmann, H. B. 2019
 Botkin, C. 252
 Boulanger, P. A. 486,
 2404
 Bourali, C. 443
 Bourali, M.-F. 853
 Bourgaux, P. 494
 Bourgaux-Ramoisy, D. 494
 Bouroncle, B. A. 1611
 Bourret, J. 371
 Bourse, R. 734
 Boush, G. M. 625
 Boutibonnes, P. 2121,2296
 Boutwell, R. K. 1817,1921
 Bowen, J. M. 1625,2014,2456
 Bowman, B. G. 1628
 Boyce, W. H. 722
 Brachmann, I. 1478
 Brada, Z. 754
 Bradley, R. M. 515
 Bradshaw, E. 901,928,
 1656,1689,2542
 Brady, J. M. 1434
 Brady, R. O. 515
 Brailovsky, C. 516
 Bralow, S. P. 1875
 Branca, M. 1430
 Brand, I. 2300
 Brand, K. G. 2300
 Brändli, O. 2526
 Bras, G. 884
 Braude, V. I. 2073
 Braun, A. 653
 Braunwald, J. 2498
 Bray, P. F. 2104
 Braylan, R. C. 1572
 Breedis, C. 1327,1609
 Bremberg, S. 300
 Bresch, H. 1564
 Bresciani, F. 155
 Breslavskii, A. S. 2226
 Bresnick, E. 1206,2325
 Bresson, J.-R. 370
 Bresson, M.-L. 2302
 Briand, P. 553
 Bricout, F. 2005
 Brière, N. 1885,2258
 Brieux de Salum, S. 978
 Brill, E. 738
 Brilliantine, L. 33
 Brisou, J. 601
 Brittinger, G. 1201
 Brobst, D. F. 1268
 Brocco, D. 1786
 Brodey, R. S. 447
 Brodsky, I. 154,261
 Brooke, B. N. 2655
 Brookes, P. 232
 Brooks, R. E. 153,1991,2332
 Bross, I. D. J. 2100
 Broustet, A. 2151
 Brown, C. D. 1010
 Brown, D. 116
 Brown, D. E. 151
 Brown, E. R. 2052,2136
 Brown, E. V. 63
 Brown, G. B. 618,1189
 Brown, H. D. 55
 Brown, J. 241
 Brown, J. K. 1030
 Brown, J. M. 1831
 Brown, M. 1288,2434
 Brown, M. M. L. 558
 Brown, O. E. 140
 Brown, R. C. 1459
 Brown, R. R. 70,1162,1484
 Bruce, D. L. 888
 Bruce-Chwatt, L. J. 1960
 Brucher, J. M. 1424
 Bruchmüller, W. 1670
 Brues, A. M. 1543,1753,
 2124,2299
 Bruevich, T. S. 2211
 Brun, J. 1044
 Brunet, M. R. 328,1605,2521
 Bryan, G. T. 71,407,426,
 427,1162,1510,1548,1556,
 1780,1781,1906,1907,1908,
 1832
 Bryant, P. J. 1194
 Bryon, P.-A. 369
 Bryson, G. 1544,1936
 Bubeník, J. 109,280,789
 Buck, B. M. 803
 Bucovaz, E. T. 1184
 Bucz, B. 322
 Buffett, R. F. 1626
 Bulay, O. M. 2329
 Bulba, A. 1974
 Bullerman, L. B. 1104
 Buncher, C. R. 930,1029
 Bundschuh, M. 2520
 Bunnag, B. 838
 Buoen, L. C. 2300
 Buraczewski, J. 339
 Burbank, F. 2544
 Burch, P. R. J. 13
 Burdette, W. J. 517,1698,2118
 Burdman, D. 1036
 Burdon, R. H. 2281
 Burger, M. M. 505,1326
 Burk, D. 1545
 Burke, J. G. 2412
 Burkhalter, A. 1205
 Burki, H. R. 210,649
 Burkitt, D. P. 885,2520
 Burlingham, B. T. 1320
 Burmester, B. R. 511,2149
 Burnery, S. W. 70,690,1484
 Burns, F. J. 1038
 Burns, W. H. 2024
 Burnstein, T. 2006
 Burr, K. 33
 Burrell, R. J. W. 1386
 Burroughs, M. A. K. 824
 Burrows, T. W. 352
 Burstein, N. A. 411
 Burtin, P. 523
 Buscheck, F. T. 150,151
 Bushar, H. F. 87
 Bushnell, D. E. 2256
 Bussey, H. J. R. 2654
 Butel, J. S. 2419,2421
 Butler, W. H. 185,363
 Buu-Hoï, N. P. 330,386,619,1084,
 1546,1861
 Byatt, P. 2632
 Bykovskii, A. F. 2022,2459
 Byrd, B. L. 1775
 Cacciari, P. 707,1725
 Cachin, Y. 523
 Caiafa, P. 976
 Cajone, F. 2262
 Calafat, J. 816,818,2399
 Calmettes, C. 1705
 Calnek, B. W. 508
 Calvert, J. 2286
 Calvoer, R. 244
 Came, P. E. 823
 Camerini, E. 628
 Cameron, H. M. 134
 Cameron, L. 889
 Campbell, L. V., Jr. 1354
 Campbell, T. C. 750,1116,1938
 Campbell, W. F. 1579
 Campobasso, O. 724
 Candeli, A. 603
 Canepari, C. 683
 Canivet, M. 805

Cantaboni, A. 1492
 Carter, H. Y. 73
 Carter, C. R. 1929,2245
 Catuti, V. 1786
 Cebalere, P. 238,1080
 Ceborio, G. 77
 Ceboron, A. 395
 Cerasievici, E. 306
 Cebone, P. P. 62
 Cediff, R. D. 1627,2398
 Cedini, G. 954
 Cey, J. J. H. 2590
 Celles-Trochain, E. 2152
 Celton, W. W. 2649
 Cenes, W. H. 1628
 Celoline, N. L. 1321,1971
 Celon, G. A. 1414
 Cep, R. I. 2451
 Cer, H. W. 1155
 Cretti, D. 683
 Cerri, J. 1669
 Cestens, L. A. 2308
 Ceter, A. P. 2528
 Ceter, B. J. 2660
 Ceter, R. L. 38,39,53,
 233,606,607,1103,1216,
 2315
 Ceton, G. P. 1786
 Ccinelli, N. 913
 Ce, R. A. M. 1119
 Ccasi, E. 863
 Ccsidy, J. T. 2639
 Ccsingena, R. 853,1278
 Ccto, B. C. 844,1308,
 1315
 Cctor, C. W. 1418
 Ccaldo, E. 1072
 Cctan, A. 2302
 Ccazzuti, F. 990
 Ccin, J. C. 1082
 Ccerqvist, L. 1664
 Cclowski, W. S. 437,765,
 1306,1571
 Cclier, K. M. 2611
 Ccilli, G. J. 1472
 Ccarini, J. P. 862
 Ccbot, J. F. 1577,1994
 Cchinian, P. 1451
 Cci, C. K. 2644
 Cci, L. S. 2035
 Cckrabarty, A. K. 765,
 1306,1571
 Ccmeaud, J. 2171
 Ccmorro, A. 264,416,
 1218
 Ccmppy-Hatem, S. 387
 Ccn, P. C. 1513
 Ccn, S. P. 1590,2370
 Ccndra, S. 150,151,1614
 Ccndrasekhara, N. 1939
 Ccng, S. S. 2369
 Ccng, P.-H. 1861
 Ccny, C. 111,462,467
 1955
 Ccpenko, S. V. 2365

Chaplin, M. D. 1061
 Chapman, A. L. 756,2112
 Chapman, W. H. 1171
 Charney, J. 474,475,822,1593
 Charpin, J. 1482
 Charuzy, I. 696
 Chassagnon, C. 1741
 Chatelin, C. L. 596
 Chattopadhyay, S. K. 55
 Chaudhry, A. P. 1075,1814
 Chaudron, J. M. 1726
 Chavez, R. F. 2229
 Chayen, J. 2271
 Chen, C. C. 1562,2251
 Chen, L. 58
 Chen, K. P. 2567
 Chen, T. T. 226,348,1065
 Cherepavova, A. I. 2216,2217
 Cherkasskii, L. A. 2231
 Chermann, J.-C. 266,1569,1977
 Chernina, L. A. 1491
 Chernov, O. V. 1778
 Chessin, L. N. 1407
 Chesterman, F. C. 1216
 Chevalier, H.-Y. 207
 Chiang, T. 2064
 Chiga, M. 1179
 Chigirinskii, A. E. 2433
 Chigot, J.-P. 1705
 Chihara, G. 1771
 Chin, T. D. Y. 2093
 Chirico, G. 326
 Chirigos, M. A. 97,270,1590,
 2370
 Chistiakova, Z. M. 1180
 Chivu, V. 1750
 Chlap, Z. 1272
 Choi, N. W. 2579,2580
 Chook, E. K. 1013
 Chopra, H. C. 293,1598,1990,
 2000
 Chou, M. W. 740
 Chouroulinkov, I. 45,732,1070
 Chretien, P. 1393
 Christian, I. 222,223,224
 Christie, G. S. 1533
 Christodoulides, L. 1777
 Christopherson, W. M. 135,2571
 Chrzanowski, A. 528
 Chu, E. H. Y. 1804
 Chuat, J.-C. 108,1624
 Chubb, R. C. 832
 Chumakov, M. P. 2440
 Chung, M. 785,2036
 Church, R. B. 1427
 Churchill, A. E. 832
 Churchill, W. H., Jr. 655
 Churg, J. 679
 Cikes, M. 446
 Cinque, G. 1679
 Cioli, V. 1463
 Cioloca, L. 221
 Citoler, P. 633
 Ciufecu, E. 2371
 Clack, J. C. 1098

Clademenos, T. 661
 Clagett, O. T. 2670
 Clapp, N. K. 1147,1547
 Clark, H. F. 471,2497
 Clark, R. L. 143
 Clark, W. R. 840,841
 Clarke, J. K. 1998,1999,2393
 Clarke, M. A. 40,1900
 Clarke, W. J. 26
 Clarkson, B. D. 921
 Clasen, R. A. 1849
 Claude, A. 307
 Claunch, B. C. 1408
 Clausen, K. P. 949,1611
 Clayson, D. B. 724,993,2253
 Clayton, J. 2570
 Clemens, J. A. 54
 Clement, C. 1745
 Clemente, R. 954
 Clemmesen, J. 574,936
 Clifford, J. I. 667
 Clifford, P. 158,509,523,826,827,
 828,1719,2039
 Clouse, J. A. 396
 Clymer, R. 2047
 Cocuzza, G. 1271
 Codegone, M. L. 418,665,1145,1487
 Coeur, P. 369
 Coezy, E. 1503
 Coffey, C. B. 1852
 Coffin, A. 33
 Coggin, J. H., Jr. 845,846
 Coghill, S. L. 2424
 Cohen, A. 1106
 Cohen, H. 756,2046,2112
 Cohen, M. H. 773
 Cohen, S. M. 426,427,1510,1548,
 1906,1907,1908
 Cohn, M. 1988
 Cohn, S. 1358
 Colburn, N. H. 1921
 Colby, C. 276,2386
 Cole, H. 884
 Cole, L. J. 1081
 Cole, P. 335
 Coleman, N. 156
 Colnaghi, M. I. 77,608
 Colombies, P. 2152
 Colten, H. R. 1578
 Commins, B. T. 32
 Commoner, B. 1848
 Condit, P. T. 1295
 Congdon, C. C. 1311
 Conklin, J. W. 1749,1754
 Consigli, R. A. 860
 Cook, M. K. 91,877
 Cook, P. 1369
 Cooke, E. M. 2178
 Cooke, R. A. 693,2532
 Cooper, E. H. 536,922,993,1167
 Cooper, P. 2570
 Cooper, R. C. 534
 Cooper, W. C. 1292
 Coppey, J. 443
 Cordero Funes, J. 2108

- Cornell, R. 981
 Correa, P. 329,1390
 Corson, S. L. 907
 Cosgrove, G. E. 589
 Costarelli, A. 1271
 Coune, A. 44
 Counts, W. B. 46
 Court Brown, W. M. 952
 Cousin, J. 1447
 Covelli, V. 1459
 Cowan, D. M. 1523
 Cowdell, R. H. 1658
 Cowen, D. M. 724,1167
 Cox, B. 197,1933
 Cox, C. E. 722
 Cox, D. E. 918
 Coyle, M. 1011
 Craddock, V. M. 1144, 1872
 Craig, A. W. 1147,1547
 Craig, R. L. 1066
 Cralley, L. J. 1764
 Cramer, R. 498
 Crawford, A. M. 1807
 Crawford, G. L. 984
 Crawford, M. A. 1368
 Creaven, P. J. 1797
 Cremer, N. E. 439,768,
 1629,2356
 Crist, S. B. 1168
 Crocker, T. T. 1795,2287
 Crofton, E. C. 1659,2536
 Croissant, O. 2473
 Croisy-Delcey, M. 619
 Cronin, M. T. I. 2249
 Crooks, J. 333
 Crosswhite, L. 2635
 Croveti, A. J. 426
 Crumpacker, C. S. 503
 Cudkowicz, G. 2343
 Cuello, C. 1390
 Cuenca, C. R. 1400
 Cuq, J.-P. 961
 Curchod, A. 356
 Cure, S. F. 768,1629
 Currie, A. R. 1807
 Cusumano, C. 838
 Cuzin, F. 2469
 Czarnomska, A. 983

 Daams, J. H. 481,2399
 Dabbert, A. F. 1370
 Dabrowski, S. 90
 Daehnfeldt, J. L. 553
 Daftary, D. K. 935
 Dagle, G. E. 841
 Dahlin, K. 2520
 Dahlin, L. 2520
 Dahme, E. 1519
 Dais, C. F. 1184
 Dallenbach, F. 521
 D'Alonzo, U. 964
 Dalquen, P. 1370
 Dalton-Tucker, M. F. 1281,
 1282
 Damel, A. 2108

 D'Angostino, F. 2096
 Daniel, M. D. 513,2040,2041,
 2042
 Daniel-Moussard, H. 181
 Dannenberg, H. 246,1478
 Dao, T. L. 376,1069,711
 Daoust, R. 1495,1549,1885
 Darnell, J. E. 1283
 Darner, E. M. 1611
 Da Silva, D. J. 1064
 Datta, S. P. 1068
 Dauber, W. 1530
 Daudel, P. 619
 Dausset, J. 1437,2594
 Dauty, A. 1762
 Davey, D. A. 908
 Davidsohn, I. 2626
 Davidson, A. 1071
 Davidson, C. S. 1374
 Davidson, J. K. 182
 Davies, J. N. P. 1681,2562
 Davies, R. F. 688,1096,1097
 Davis, H. J. 2043
 Davis, R. C. 2183
 Davis, R. H. 2268
 Davis, W. C. 963,1040,1618
 Davison, B. C. C. 886
 Davydenko, V. A. 2669
 Dawson, K. M. 2253
 Dawson, P. J. 106,436,769,771,
 1630
 Day, E. D. 797,1240
 Day, T. D. 688
 De Albertis, P. 994
 Dean, G. 1655
 Deaner, R. M. 2541
 De Angelis, L. 2072
 Deardorff, W. L. 2482
 De Azavedo e Silva, E. 1922
 DeBaun, J. R. 672,1550,1854
 Debray, C. 961
 Debski, T. 916,1391
 de Carvalho, A. R. L. 355
 Deckert, M. 1211
 Declève, A. 2333,2334
 DeCosse, J. J. 1197
 Defendi, V. 867,1323,1631,
 1641,1978,2448
 Degos, L. 1437,2594
 DeGowin, E. L. 30
 de Harven, E. 447,2351
 Dehnen, W. 205,643
 Deichmann, W. B. 69
 Deinhardt, F. 1249,1312,1584,
 2504
 De Jager, H. 681
 Dekegel, D. 2589
 del ande Eaton, S. 2223
 Delange, J. 189
 Delescluse, C. 1732
 Della Porta, G. 77,608
 DeLong, D. C. 265
 de Lustig, E. S. 1056
 Delwaide, P. A. 640,641
 Demaille, A. 395
 Demissie, A. 2039

 Den Engelse, L. 1870
 Dent, P. B. 763
 DeNyse, D. 1408
 Deodhar, S. D. 2064
 DeOme, D. B. 116,286,289,710,
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 de Petris, S. 2362
 Deringer, M. K. 554
 Dermott, E. 1999,2393
 DeRoche, G. M. 1543,1753,2124,
 2299
 De Rosa, M. 1679
 Dersjant, H. 391
 Desbordes, J. 1762
 de Schryver, A. 523
 de Serres, F. J. 1158
 Deshpande, V. A. 2066
 De Silva, L. M. 1109
 Dessev, G. N. 201
 de-Thé, G. 523,1632
 Detroy, R. W. 662, 2297
 de Vaux Saint Cyr, C. 313,848,
 1606,2507
 DeVita, V. T. 959
 De Waard, F. 583
 Dewhurst, F. 1092
 Deys, B. F. 2667
 d'Hooghe, M. 238,1080
 Diad'kova, A. M. 2376,2380
 Diamandopoulos, G. T. 1281,1282
 Diamond, L. 409, 1551
 Dicke, T. E. 1102
 Dickie, M. M. 250
 Dieckmann, M. 2469
 Diehl, V. 509,523
 Diengdoh, J. V. 2271
 Dienst, H. 1161
 Dietz, W. 1878
 Diggelmann, H. 794
 Dihmis, C. 543
 Dikow, A. L. 1148,1928
 Dikun, P. P. 2208,2209,2210
 Dilenno, J. 1714
 Dillard, R. D. 265,1563
 Dillingham, L. A. 700
 Di Luzio, N. R. 1416
 Dimant, I. N. 2284
 Di Marco, A. T. 1891
 Dimitrov, N. V. 261
 Dingman, C. W. 46
 Diosi, P. 1612
 DiPaolo, J. A. 36,385,1553,1859
 Dipple, A. 232
 Diringer, H. 698,2221
 Di Stefano, H. S. 1012
 Dixon, C. B. 2423,2424
 Dixon, F. J., Jr. 354,2063
 Dixon, J. A. 2552
 Dixon, J. R. 1764
 Dmochowski, L. 294,811,1600,1625,
 1984,2014,2364
 Doane, F. W. 2472
 Dobrescu, G. 1745
 Dobson, R. L. 1466
 Dodd, D. C. 469
 Dodd, M. C. 864,2058

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odonova, N. N. 2022,2413,
2430,2433
oell, R. G. 1203,1552,
2389
oerfler, W. 1320,2059
ohan, D., Jr. 2033
oi, T. 2488
oljanski, F. 1942
omschke, W. 194
onawick, W. J. 469
oniach, I. 2174
onner, L. 280
onovan, J. W. 1695
onovan, P. J. 36,385,
1553
ontenwill, W. 174,175,
176,180,207,675,687,
1799
ontschewa-Stratewa, N. 1378
oré, J.-F. 441,1570,
1574,1576,1982
oré, M. 1576
irken, H. 524,2606
orn, C. R. 969
s Santos Pinto, D. 1739
oto, I. L. 2093
ty, S. B. 1981
ugan, L. 2625
ugherty, R. M. 777,
1012
urmashkin, R. 786
usset, G. 1762
wling, A. M. 2455
wning, A. 2556
wns, W. G. 2049
aganov, I. 2199
ago, G. 2072
ash, A. 2106
echslarová, E. 2207
exler, J. 1485
layfuss, Y. 2634
liessens, J. 238,395,
1080,1082,1083
lings, P. 982
liscoll, D. H. 2612
lolette, M. 1335
lozdová, A. 754
lożdżewska, Z. 1373
lockrey, H. 637,1005,
1191,1193
lubs, D. R. 315,852,1278,
1279,2030,2434,2435,
2452
low, H. 1387
la, M. 306
chesne, J. 430
os, J. 2152
ros, M.-D. 476,477,
480
sberg, P. H. 465
of, R. G. 781,2422
o, I. L. 2383
e, G. A. 1196
ac, G. C. 1268,2006
Dulbecco, R. 10,494
Duman, M. 1458
Duncan, M. 232
Duncan, R. M. 1085
Dungworth, D. L. 1034,1964
Dunkel, V. C. 829,1633
Dunlop, W. R. 85
Dunn, G. R. 957
Dunn, J. A. 202
Dunn, J. E., Jr. 1337
Dunn, T. B. 715,1554,1599,
2628
Dunning, W. F. 1558
Duong, P.-N. 330
Dupin-Girod, S. 1769
Duplan, J. F. 361
DuPlessis, L. S. 397
DuPraw, E. J. 341
Duque, E. 1390
Durif, S. 181
Durst, A. 1076
Duryee, W. R. 2309
Dutrillaux, M.-C. 817
Dutrillaux-Ducros, M.-C. 287
Dutsić, S. 2549
Dutton, A. M. 23
Dyer, H. M. 1902
Dzagurov, S. G. 2382
Dzhioev, F. K. 724
Dziukowa, J. 339
Eagle, H. 2470
East, J. 1430
Easton, J. M. 958,1267
Easton, N. R. 265
Ebbesen, P. 973,1232
Ebert, J. 2112
Ebert, J. S. 455
Ebert, P. S. 1590, 1634
Ebner, H. 1901
Echave Llanos, J. M. 2617
Eckenhoff, J. E. 888
Eckert, L. 1835
Eckhart, W. 580
Eckner, R. J. 1975
Edlin, G. 2386
Edward, V. D. 692
Edwards, L. D. 733
Efimov, V. P. 2666
Eggemann, G. 1670
Eguchi, M. 1468
Ehrenreich, T. 2634
Ehrentaut, W. 249
Eichel, B. 413
Eide, K. A. 888
Eilber, F. R. 1591
Eisenberg, H. 909,2094
Eisenstein, S. 759
Eisenstein, Z. 883
Elashoff, R. M. 21
Elekoiev, K. A. 2382
Elguin, G. H. 985
Eligulashvili, R. K. 2365
Elkeles, A. 2110
Elliott, A. M. 1483
Elliott, S. C. 617
Ellsworth, P. A. 1634
Elmenhorst, H. 174,175,176,675
Elmer, I. 49
Elrod, L. H. 845
El-Shafei, A. K. 1099
Elveback, L. R. 338
Elzay, R. P. 1802
El-Zoghby, S. M. 1099
Emafo, P. O. 1114
Emanoil-Ravicovitch, R. 1246
Emmelot, P. 1870
Emshanova, A. V. 2208,2209
Encut, I. 221
Endo, H. 1468,1862
Eneroth, C.-M. 2584
Engel'gardt, N. B. 2348
Engle, C. G. 52
Engstrom, G. W. 79
Enomoto, H. 2166
Enterline, P. E. 2539,2540
Epstein, A. 300
Epstein, L. I. 1331
Epstein, S. M. 61,671,1845
Epstein, S. S. 164,1555,1779
Epstein, W. L. 1996
Erb, P. 2407
Erb, R. J. 2186
Erdős, Z. 1348
Erikson, E. 2054
Erikson, R. L. 2054
Ernault, J.-L. 1762
Erokhin, R. A. 2176,2177
Ershoff, B. H. 1461
Ershova, K. P. 1827
Ertürk, E. 407,426,427,1510,
1556,1780,1906,1907,1908
Esber, H. J. 2317
Escalera, G. A. 2306
Eshleman, L. 885
Estampe, B. 2594
Estes, J. D. 2392
Estrade, S. 853
Étienne, J.-P. 961
Eugster, A. K. 457
Evans, A. E. 1566
Evans, A. S. 1256
Evans, C. A. 308
Evans, M. J. 2408
Evans, V. J. 346
Everett, M. A. 1295
Evers, C. G. 552
Ezdinli, E. Z. 1405,1460,2635
Fabia, J. 1335
Fábián, B. 604
Fabian, F. 2497
Fabiani, A. 1880,1881,2283
Fabrikant, J. I. 1420,2164,2614
Fadda, G. 109,279,1234
Faed, M. J. W. 956
Fahmy, M. J. 382,1182,1760,2289
Fahmy, O. G. 382,1182,1760,2289

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1095,2301
 Falor, W. H. 684
 Fantini, F. 1492
 Farber, E. 61,671,1845
 Farmilo, A. J. 861
 Farooki, M. A. 584
 Fasske, E. 311
 Faucounau, N. 429
 Faulkin, L. J., Jr. 819
 Fechner, R. E. 1126,1806
 Fefer, A. 808,1589,1635
 Fehr, P.-M. 189,572
 Feinleib, M. 1388
 Fekety, F. R., Jr. 2590
 Feldman, D. G. 1644
 Feller, W. F. 293
 Felluga, B. 307
 Fendell, L. D. 2313
 Fenton, A. N. 1358
 Fenyő, E. M. 438
 Ferber, K. H. 545
 Ferguson, D. B. 518
 Fernandes, G. 1190
 Ferrans, V. J. 350
 Ferrante, W. A. 1457
 Ferrea, E. 1707
 Ferreira-Salgado, M.-A. 857
 Ferrer, J. F. 445,1636
 Ferrero, M. E. 2262
 Fetting, R. 311
 Fey, F. 263,1223,1224,
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 Fiala, S. 12,652
 Fialkow, P. J. 1394
 Fichidzhian, B. S. 273
 Fickling, B. W. 1419
 Fiel, R. J. 125,1637
 Field, A. K. 512
 Field, E. J. 103
 Field, J. B. 1461
 Fields, C. 2136
 Fieldsteel, A. H. 106,436,769,
771,1630
 Fienberg, R. 548
 Fierz, L. 129
 Figge, F. H. J. 1981
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 Fink, L. M. 2250
 Fink, M. A. 773,2491
 Finkelstein, S. 547
 Finlayson, N. D. C. 1045
 Finzi, C. 1801,1891,1892
 Fischer, H. 1286
 Fischer, P. 546
 Fischinger, P. J. 272,452,459,
460,806,1638,2359
 Fish, F. 1765
 Fishbein, L. 31,410
 Fisher, B. 146
 Fisher, E. R. 146,1233
 Fisher, J. C. 2183
 Fitzgerald, P. H. 934
 Fitzpatrick, W. K. 1687
 Fjelde, A. 1710
 Flaks, A. 60,1462,1897,2188
 Flaks, B. 60,64,1897
 Flehinger, B. J. 1387
 Fleissner, E. 1313,1728,2374
 Fletcher, C. M. 737
 Fletcher, R. 2220
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 Flowers, A. 320
 Floyd, R. 2061
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 Forni, A. 951
 Förström, L. 595
 Fort, L. 971,1424
 Foster, J. A. 627
 Fournaud, S. 1769
 Fournier, A. 1447
 Fouts, J. R. 1090
 Fox, H. 1357
 Fox, R. R. 1231
 Foy, H. 970
 Fraley, E. E. 506
 Franceschi, C. 1801,1892
 François, D. 1588
 Frank, H. 1952
 Franke, R. 1783
 Franklin, R. 2555
 Franko, M. 118
 Franks, L. M. 152
 Fraser, C. E. O. 2040,2041,
2042
 Fraumeni, J. F., Jr. 131,316,
585,586,914,926,933,958,959,
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 Friedmann, I. 568,704
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 Frischauf, H. 211
 Fritsch, S. 813,1989
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 Frohwirth, N. 2221
 Frolov, A. F. 1619,2291
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 Fudenberg, H. H. 1040
 Fujii, K. 1779,2264
 Fujimura, S. 1465,1874
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 Fukuda, S. 1490
 Fukui, K. 1259,1262
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 Fukuyama, K. 1996
 Fullmer, C. D. 2319
 Fulton, R. E. 2472
 Funk, C. A. 122
 Furer, N. M. 2346
 Furst, A. 996,1559
 Furuno, A. 1289
 Furuya, M. 613
 Fuse, Y. 2154
 Fushimi, K. 2314
 Gadekar, K. 252
 Gadowska, H. 1373,2524
 Gadrat, J. 734
 Gaffney, E. V. 847,1300,1317,
1604,1639,2453,2455,2509
 Gahlen, W. 1717
 Gaja, G. 2262
 Galea, V. 161
 Galetti, G. 730,1492
 Gallager, H. S. 294,538,1600
 Gallagher, T. F. 1412
 Gallien-Lartigue, O. 99
 Gallina, F. 326
 Gallmeier, W. M. 2037
 Gallo, R. C. 1968
 Gamble, C. N. 144
 Gamburg, V. P. 2429
 Gandagule, V. N. 2531
 Gangadharan, P. 2067
 Gangolli, S. D. 699
 Gantt, R. C. 931
 Garbe, E. 2521
 Garbut, A. 1091
 García, F. G. 2040,2041,2042
 García, H. 712,1187
 García, J. S. 2593
 García-Giralte, E. 456
 Gardner, D. 1560
 Gardner, L. I. 2316
 Gardner, M. B. 2392
 Gardner, M. J. 2537
 Garfinkel, L. 178
 Gargus, J. L. 676,701
 Garnier, H. 1705
 Garon, C. 150,151
 Garrafa, V. 1739
 Garret, M. 1036
 Garrett, T. 209
 Garrison, R. J. 1388
 Gart, J. J. 31
 Gasparoni, M. C. 1702

- Gasser, U. 2672
 Gaston, M. 1635
 Gates, O. 1758
 Gautheron, D. 1610
 Gavankar, M. H. 1253
 Gavitt, F. 1312
 Gavosto, F. 1446
 Gay, F. W. 1999,2393
 Gaylor, J. L. 1060
 Gazdar, A. F. 2367
 Geering, G. 447,2489
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 Gentile, J. M. 1972
 Gentilhomme, O. 369
 Gergescu, D. C. 2515
 Gergii, A. 866
 Gerales, A. 491,1270
 Gerardi, Q. 327
 Gerber, M. 2052
 Gerber, M. A. 1763
 Gerber, P. 2143,2480,2482
 Gergely, L. 1617
 Gerke, G. 663
 Gerstley, B. J. S. 2591
 Gertman, P. M. 2279
 Gerwel, T. 172
 Giali, F. H. 1366
 Gelelelovitch, S. 27
 Getti, G. 683
 Gittino, P. 418,665,1487
 Glose, T. 1068
 Gosh, A. K. 75,1642
 Gosh, I. 2630
 Gosh, S. 2630
 Gao, N.-B. 386,416,1546
 Gabs, F. 1636
 Gabs, F. A., Jr. 445
 Gabs, G. W. 32
 Gabel, W. 162,163,1720
 Gablett, E. R. 1394
 Gabsen, R. 2592
 Gabsen, W. R. 1563
 Gchner, T. 741
 Gnoux, M. 368
 Gbartsen, V. A. 1344
 Gden, R. V. 463,484,801,
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 2369,2390,2588
 Ggen, A. 2214
 Glette, K. G. 470
 Gman, J. P. W. 1177,1178
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 Gmour, J. 2557
 Gnsberg, H. S. 2055,2056,2400
 Gordan, G. 1725
 Gorgi, R. 1113
 Govanella, B. C. 2157
 Gard, M. 2031
 Gard, R. 369,371,372
 Gardi, A. J. 1641
 Gari, C. P. 621
 Gisin, S. 1235
 Gitlin, D. 62
 Gitter, S. 2267
 Glade, P. R. 1407
 Glass, A. G. 1345,1682
 1700
 Glass, R. M. 2249
 Glick, J. L. 1257
 Glover, E. L. 213,420,1050
 Gnosselius, Y. 2204
 Godbole, V. K. 1364
 Goetz, I. E. 1561
 Gofman, J. W. 1748
 Gogichadze, G. K. 579
 Gold, E. 316
 Goldberg, M. 2265
 Goldberg, M. L. 950
 Goldblum, N. 2026,2027,2062
 Goldé, A. 784,2381
 Goldenberg, D. M. 1233,2664
 Goldenberg, H. 938,1825
 Goldfeder, A. 75,1642
 Goldin, A. 1993
 Goldman, A. 1513
 Goldman, M. 87,1034,2255
 Goldner, H. 767,1316,1603
 Goldschmidt, B. M. 419,1784
 Goldstein, D. 495
 Goldstein, D. P. 947
 Goldstein, G. 826
 Goloviznin, G. I. 2376
 Golub, E. 546
 Golub, N. I. 1470
 Good, R. A. 431,763,1198
 Goodall, C. M. 185,1712
 Goodheart, C. R. 9
 Goodman, E. S. 303
 Gordon, D. E. 1269
 Gordon, H. L. 125
 Gordon, L. S. 1926
 Gordon, M. 684
 Gordon, T. E., Jr. 1926
 Gorelova, N. D. 2216,2217
 Gori, G. B. 980
 G6rlich, M. 2228
 Gorodilova, V. V. 2413
 G6rski, T. 1021
 Gosch, H. H. 199
 G6ssner, W. 195,400
 Gothoskar, S. V. 690,1190
 Gotlieb-Stematsky, T. 979
 Gotoh, A. 2038
 Gotoh, S. 1143
 Gott, C. 1582
 Grabar, P. 313,848
 Graber, E. A. 557
 Grace, J. T., Jr. 1227,
 1626,1633,1643,2035
 Graf, T. 789
 Gräf, W. 1796
 Graffe, L. H. 1285
 Graffi, A. 488,1805
 Graham, J. B. 2568
 Graham, S. 2592
 Grahn, B. 1243
 Grahn, D. 2178
 Gralnack, H. R. 1407
 Granados, R. R. 321
 Granata, A. 2072
 Grand, L. 1829
 Grande, P. 1668
 Grant, G. A. 611,702,703
 Grantham, P. H. 433,434
 Grasso, P. 351,609,699
 Gravelle, C. 2112
 Gray, C. 2497
 Green, B. 747
 Green, C. H. 1822
 Green, G. H. 1695
 Green, H. 2461
 Green, M. 514,835,1260,2145
 Greenawalt, C. 451
 Greenberg, R. A. 909
 Greenblatt, M. 363,1759
 Greenlaw, R. H. 588
 Grégoire, A. 462,467
 Gregor, O. 1432
 Greisen, O. 1426
 Grendon, A. 1835
 Gresser, I. 443
 Gretskaia, O. P. 2208,2209
 Griesback, L. M. 2185
 Grieshaber, E. 250,1251,1298
 Griffin, A. C. 255
 Griffin, W. 97
 Griffiths, K. 4 2
 Grilli, S. 1524
 Grimes, R. A. 151
 Grimstvedt, M. 1077
 Gripenberg, U. 58
 Grismond, G. L. 1798
 Griswold, D. P., Jr. 1822,1824
 Grogan, D. E. 2285
 Groot, 2278
 Grosdidier, J. 360
 Gross, J. 2175
 Gross, K. 911,2646
 Gross, L. 1644,2634
 Gross, S. 2564
 Grosse, H. 891
 Grossi-Paoletti, E. 1880,1881,2283
 Grosso, E. 325
 Groth, D. H. 678
 Groupé, V. 52,2379
 Gr6zinger, K.-H. 521
 Grubb, C. 987
 Grube, D. D. 1543,1753,2124,2299
 Gruenstein, M. 212,1823,1825,1875
 Grunberg, E. 605
 Grunberger, D. 1929,2245
 Grundmann, E. 1894
 Gsell, O. 128
 Gubareva, A. V. 1744
 Gubeladze, D. A. 2406
 Gueguen, S. 1511
 Guentzel, M. J. 2419
 Guérin, M. 45,732
 Guerrero, A. 712
 Guest, B. A. 2576
 Guillemain, B. 807
 Guillon, J.-C. 732,1070
 Guir, J. 2498

- Gullen, W. H. 2579,2580
 Guminska, M. 553
 Gunner, S. W. 403
 Gunnlaugsson, G. H. 2670
 Gunvén, P. 108
 Gunz, F. W. 1911
 Gupta, P. C. 935
 Gupta, P. K. 705
 Gurda, M. 1392,1397,2595
 Gurtoo, H. L. 1116
 Gurtsevich, V. E. 2354
 Gusberg, S. B. 1136
 Gusek, W. 719,1774
 Gutmann, H. R. 3,1562,
 2242,2251
 Guttman, P. H. 1040

 Haas, R. 1751
 Haase, A. T. 1407
 Haber, M. H. 2074
 Hacker, B. 1319
 Hackett, A. J. 2398
 Hadjiolov, D. C. 1148,1928
 Haenszel, W. 1338,2066
 Haerer, A. F. 552
 Hafeez, M. A. 2573
 Haga, M. 2314
 Hageman, P. C. 816,818
 Hågerstrand, I. 966
 Hagmar, B. 622,1469
 Hagopian, M. 173
 Haguénau, F. 454,787
 Hahn, E. C. 2025,2446,
 2454
 Hahn, G. M. 2333,2334
 Haidak, G. L. 2159
 Hairstone, M. A. 1292
 Hakama, M. 1380
 Hall, R. H. 2029
 Hall, W. T. 468,478,815,
 1592
 Halliday, W. J. 51
 Halver, J. E. 666
 Hamajima, K. 2038
 Hamann, W. 34
 Hamazaki, Y. 2318
 Hamburg, V. P. 119,2418
 Hamer, J. W. 934,1911
 Hamilton, J. M. 1462
 Hamilton, P. B. 749
 Hamilton, T. 1041
 Hammerling, U. 2351
 Hammond, E. C. 178,900,
 1355,1444,2071
 Hammond, W. G. 43
 Hampar, B. 824,2480
 Hampe, A. 807
 Hampton, S. 798
 Hanada, M. 1139
 Hanafusa, H. 2385
 Hanafusa, T. 2385
 Hanaki, A. 1137,2260
 Hanaoka, M. 1428
 Hancock, R. 493,2144
 Hancock, R. L. 250
 Handa, H. 1879
 Handa, J. 1879

 Handrache, L. 306
 Hanks, C. T. 1075
 Hanna, M. G., Jr. 2349
 Hansen, I. L. 1368
 Hanson, J. 1835
 Hanson, L. E. 490
 Hansteen, I.-L. 1514,1515
 Haran-Ghera, N. 58
 Harbers, E. 982
 Hardy, W. D., Jr. 447
 Hare, J. D. 1608,2458,
 2464
 Harington, J. S. 1713,
 2122
 Harke, H.-P. 174,175,176,
 180,675,687,1799
 Harley, E. H. 1106
 Harlow, R. A. 1037
 Harnden, D. G. 83,952,
 956
 Haro, R. T. 996
 Harris, A. W. 2640
 Harris, C. 1210
 Harris, C. C. 1179
 Harris, J. W. 1701
 Harris, P. N. 1563
 Harrison, L. H. 722
 Harrold, J. B. 1964
 Harse, J. 412
 Hart, E. R. 31
 Hart, M. L. 1628
 Hartenstein, R. 204,1534
 Hartley, J. W. 440,442,
 458,2353
 Hartley, M. W. 2643
 Hartman, P. A. 1104
 Hartmann, P. 1645
 Hartmann, W.-H. 2106
 Hartwell, J. L. 1022
 Hartwich, G. 1120
 Harvey, J. J. 2362
 Hashida, C. 1772
 Hashimoto, Y. 1889
 Hass, G. M. 1849
 Hata, S. 353
 Hata, Y. 1455
 Hatanaka, M. 463,1959,
 2360,2369
 Haughton, G. 1009,1209
 Hausknecht, R. U. 1136
 Hay, D. 760
 Hayashi, K. 2665
 Hayashi, M. 2260
 Hayat, M. 2302
 Hayes, R. L. 1775
 Hayhoe, F. G. J. 1438
 Hayry, P. 1323,1978,
 2448
 Hays, E. F. 102,1646
 Hayward, A. F. 1419
 Heath, C. W., Jr. 917,
 1678,2593
 Heber, J. 130
 Hebert, G. J. 1177
 Hecker, E. 208,1564
 Hecker, W. 2443,2444,
 2445

 Heidelberger, C. 226,348,388,
 698,1065,2123,2155,2185,
 2221
 Heimann, R. 44
 Heimback, R. D. 1038
 Heine, K.-M. 1423
 Heine, U. 779
 Heinecke, H. 813
 Heise, E. 2228
 Heisler, H. 521
 Heller, J. R. 1721
 Hellman, A. 549
 Hellman, K. B. 549
 Hellman, L. 1412
 Hellriegel, K. P. 1406
 Hellström, I. 308
 Hellström, K. E. 308
 Helmboldt, C. F. 870
 Hempelmann, L. H. 23,2173
 Hems, G. 179
 Henderson, E. S. 1225
 Henderson, J. S. 1565
 Henderson, W. J. 412
 Henle, G. 509,523,826,827,1443,24
 Henle, W. 509,523,826,827,1443,24
 Hennings, H. 1817
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 Herberman, R. B. 855,2457,2505
 Herbertson, R. M. 1352
 Herbet, A. 848
 Herman, B. 2540
 Herranz, G. 1869
 Herrold, K. M. 187,1154
 Herron, J. 1381
 Hertenstein, C. 2037
 Hertz, R. 2
 Herz, A. 761
 Herz, E. 1704
 Herzog, 866
 Hesseltine, C. W. 662,2297
 Heuson, J. C. 44
 Hewetson, J. F. 1617,2379
 Heyden, S. 532
 Heyl, T. 2527
 Hiasa, Y. 243,1156,2235
 Hicks, C. 1192
 Hicks, R. M. 2254
 Hienz, H. A. 1201
 Higashi, K. 1143
 Higashino, S. 2111
 Higginson, J. 2561
 Highman, B. 1692
 Hilf, 938,1825
 Hill, B. J. 2651
 Hill, B. R. 1561
 Hill, C. S. 143
 Hill, H. C. 2266
 Hilleman, M. R. 512,840,841,842
 Hillström, L. 2529
 Hilton, C. 2105
 Hiltz, J. E. 1042
 Himuma, Y. 2012
 Hino, S. 1242
 Hinuma, Y. 296

- Hinz, I. 1370
 Hinz, R. W. 785
 Hinz, H. C. 2475
 Hirai, M. 1052
 Hiraki, K. 260
 Hiramatsu, T. 1156
 Hirano, S. 437,766
 Hirayama, T. 126,1675,2038,
 2596,2599
 Hirohata, T. 1662
 Hirokawa, Y. 268
 Hirono, I. 2314
 Hirose, F. 167,1672
 Hirsch, M. S. 875,876
 Hirschman, S. Z. 272,806
 Hirumi, H. 321
 Hitchner, S. B. 508
 Hitosugi, M. 2538
 Ito, I. J. 456
 Ito, H.-C. 523,1632
 Ito, D.-D. 330
 Ito, M.-Schneegg, B. 1941
 Ito, K. 1474
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 Ito, M. E. 1035
 Ito, R. J. 1248
 Ioffman, N. R. 2551
 Ioffmann, D. C. 35,2655
 Ioffmann, H. D. 2206
 Ioffmann, M. 399,1149
 Iolden, H. T. 118
 Iolland, J. F. 1330
 Iollande, E. 287,476,480,
 817
 Iollinshead, A. 838,2003,
 2405
 Iollmann, K. H. 291
 Iollmberg, E. A. D. 1032,
 1454
 Iolmes, E. C. 657
 Iolmes, H. L. 1031
 Ioltz, J. L. 678
 Iolzmann, H. 1704,2153
 Iolzner, H. 546
 Iomburger, F. 384,1214,
 1816,2097
 Iomer, R. B. 747
 Ionda, Y. 1006
 Iok, R. H. 2312
 Iok, W. A. 2370
 Ioson, J. 699
 Iopewell, J. W. 234,1094
 Iopkin, I. D. 1037
 Iorák, J. 1715
 Ioribata, K. 2640
 Iorikawa, M. 1865
 Iorn, D. 166
 Iorne, M. K. 84
 Iroszewicz, J. S. 1633,
 2035
 Irowitz, I. 2539
 Irsch, A. 972
 Irtton, R. E. 433,434
 Ishino, H. 229,1151,
 1771
 Ishino, K. 1997
 Ishino, T. 19
 Hosoi, H. 1151
 Hosokawa, A. 613
 Hosokawa, M. 100,764,
 2341
 Hossfeld, D. K. 1727
 Howard, B. V. 314
 Howard, E. B. 26
 Howard, T. 1545
 Howe, C. D. 869
 Howell, B. A. 197
 Howell, M. 989
 Howland, R. D. 1205
 Hrivňáková, A. 344
 Hruban, Z. 1341
 Hrushovetz, S. B. 894
 Hsiung, G. D. 1276,1328,
 1601,1602
 Hsu, K. C. 2480
 Hsueh, S.-S. 1816
 Huang, C. C. 2114,2262,
 2631,2663
 Huberman, E. 381,401
 Hudson, J. 495
 Huebner, R. J. 8,94,408,
 449,451,458,461,463,
 472,484,557,776,802,
 814,843,919,1220,1221,
 1222,1235,1303,1305,
 1314,1516,1573,1581,
 1965,1979,2353,2369,
 2390,2392,2405,2588
 Hueper, W. C. 241
 Huggins, C. 220,246,1829
 Hughes, P. E. 1851,1887,
 1888,
 Hughes, R. G. 1625,2014
 Huguet, J. 1447
 Hull, E. W. 62,131
 Hulse, E. V. 168,1028
 Hulu, N. 2610
 Hummelter, K. 2442,2508
 Humphrey, L. J. 1063,
 1417
 Humphrey, R. R. 2650
 Hunstein, W. 525
 Hunt, R. D. 513,2040,
 2041,2042
 Hunter, L. 1063
 Huong, B.-O. 330
 Huriaux, J. M. 2005
 Hurst, L. 416,650
 Hutt, M. S. R. 1374
 Hyman, G. A. 882
 Iakovleva, L. A. 2503
 Iancu, I. 1745
 Ibanez, M. L. 143
 Ichikawa, Y. 343
 Ichimaru, M. 2603
 Ichimura, H. 251,422,428
 Ievleva, E. S. 2348
 Iftimovici, M. 2020,2249
 Igel, H. J. 408,776
 Iijima, S. 930,1029
 Ikawa, Y. 98,268
 Ikegami, R. 1539
 Ikegami, S. 1866
 Ikegami, T. 425
 Ilbery, P. L. T. 1031,1033
 Il'inskiĭ, A. P. 1788
 Imaeda, Y. 267
 Imagawa, D. T. 1309
 Imahori, S. 1304
 Imaizumi, T. 192,196,248
 Imamura, A. 598,1867
 Imamura, N. 20
 Imamura, T. 2114,2631,2663
 Imoto, T. 1156
 Inbar, M. 312,2427
 Innes, J. R. M. 31
 Inokuchi, K. 1873
 Inomata, M. 598
 Inoue, Y. K. 2402,2403
 Invernizzi, F. 730,1492
 Ioki, Y. 598
 Ionescu, L. 306
 Ionescu-Homoriceanu, S. 1285
 Iorio, A. M. 865
 Ipsen, J. 127
 Irino, H. 2190,2665
 Irino, S. 260
 Irlin, I. S. 2459
 Irving, C. C. 1855
 Isaacs, J. J. 2490
 Isaka, H. 1864
 Isard, H. J. 912
 Ishihama, A. 1455
 Ishii, K. 304
 Ishikawa, M. 1156
 Ishimoto, A. 489,774
 Ishizaki, R. 1943
 Ishizawa, J. 230
 Ishizawa, M. 1862
 Israel, L. 1451
 Israilian, A. A. 2284
 Ito, M. 1508
 Ito, N. 243,1156
 Ito, T. 20
 Ito, Y. 88,267,302,489,925,2038,
 2187
 Itoh, K. 1169,1895
 Iudicello, P. 1605
 Iuzvinkevich, A. K. 2657
 Ivankovic, S. 637,723,1005,1191,
 1193
 Ivanova, N. A. 793,800
 Ivanova, O. Iu. 2202
 Iverson, O. H. 537
 Iwa, N. 2488
 Iwahara, S. 739
 Iwakami, T. 967
 Iwameji, Y. 872
 Iwao, M. 739
 Iype, P. T. 1065,2185
 Izard, C. 45,414
 Izzotti, S. 905
 Jablon, S. 1755
 Jabłoński, L. 1284
 Jackson, E. W. 1680
 Jackson, J. F. 552
 Jackson, J. L. 346,2628
 Jacob, A. 1138
 Jacox, H. W. 593

- Jacquemont, B. 1610
 Jacquet, J. 2121,2296
 Jacquigon, P. 619
 Jahn, U. 1840
 Jainchill, J. L. 2358,2436
 James, H. L. 1184
 Jameson, M. H. 2572
 Jamison, R. M. 2023
 Jandová, A. 550,551
 Janicki, J. 1111,2295
 Janicki, M. 1392
 Jānisch, W. 17,242,253,
 631,632,1153,1877,
 1878
 Janota, I. 987
 Janoušková, J. 1173
 Janss, D. H. 1212,1826,
 2327
 Jarrett, O. 760
 Jasmin, C. 266,1569,1977
 Jasmin, G. 725,1820
 Jasty, V. 124,833
 Jaszcz, W. 1272
 Jaume, F. 486
 Jeejeebhoy, H. F. 1512
 Jefcoate, C. R. E. 1060
 Jellema, M. R. 1830
 Jellinck, P. H. 209,2220
 Jenkins, D. C. 756
 Jenkins, T. W. 1504
 Jensen, F. C. 1631,2508
 Jensen, H.-E. 898
 Jensen, M. M. 96
 Jenson, C. B. 1351
 Jerkofsky, M. A. 1329
 Jernstrom, P. 2632
 Jewell, W. R. 1063
 Jílek, M. 1718
 Jobst, K. 37
 Jochweds, B. 337
 Joffe, A. Z. 669
 Johansson, H. 1505
 Johansson, S. 2545
 Johnson, J. 2160
 Johnson, K. H. 2300
 Johnston, B. 1434
 Johnstone, C. 469
 Jolles, B. 1658
 Jones, B. 1336
 Jones, D. W. 599,2218
 Jones, E. W. 2527
 Jones, H. B. 1839
 Jones, H. W., Jr. 1395
 Jones, J. C. 2312
 Jones, O. W. 1168
 Jones, R., Jr. 1643
 Jones, R. F. 2416
 Jones, T. C. 513
 Jonsson, N. 1244
 Jordan, R. 2622
 Josey, W. E. 2576
 Joshi, V. V. 402,1935
 Jost, R. 1918
 Joyce, G. 103
 Juberg, R. C. 1336
 Juhasz, J. 1043
 Juhls, H. 249
 Jull, J. W. 216,217,218,
 1522
 Jullien, P. 1992
 Jung, E. G. 2311
 Jungstand, W. 813
 Jussawalla, D. J. 1448,2066
 Just Viera, J. O. 2306
 Jutz, C. 1546
 Juźwiak, J. 1118
 Kachani, Z. F. C. 500
 Kaczala, O. A. 684
 Kafuko, G. W. 509,878
 Kagabu, T. 1455
 Kahan, B. D. 657
 Kaiser, R. 1690
 Kaji, H. 764
 Kajima, M. 575,731,790,
 1301
 Kakefuda, T. 1896
 Kaliev, Y. 850
 Kalima, T. B. 1379
 Kalinina, I. A. 1792,
 2210
 Kalinovsky, T. 288
 Kallner, G. 530,879,
 1651
 Kalman, E. 2200
 Kalnins, Z. A. 2660
 Kalomiris, C. G. 2612
 Kalter, S. S. 457
 Kamada, N. 590,591,592
 Kamei, Y. 2605
 Kamibayashi, K. 2095,2597
 Kaminetzky, H. A. 1737
 Kamiński, Z. 337
 Kamiya, H. 1969
 Kampschmidt, R. F. 2652
 Kanazawa, K. 1103
 Kanemasa, Y. 1264
 Kaneuchi, C. 620
 Kang, H. S. 2439
 Kano, T. 597
 Kantemir, I. 1078
 Kantor, I. 2162
 Kantschev, K. 522
 Kaplan, E. L. 2651
 Kaplan, H. S. 2333,2334
 Kaplan, L. 960
 Kaplow, L. S. 1328
 Kára, J. 874
 Karácsónyi, G. 1654
 Karewicz, Z. 2524
 Kariyone, S. 2167
 Karl, S. 2047
 Karmody, A. J. 1666
 Karsch, P. 2664
 Karwacka, H. 1284
 Karwowski, A. 1350
 Karzon, D. T. 2497
 Kasahara, S. 483
 Kashulina, A. P. 1502
 Kasper, T. A. 2570
 Kass, S. J. 2008
 Kastelan, A. 2196
 Katagiri, S. 2012
 Katayama, H. 2172
 Katinová, L. 874
 Kato, H. 317,2559
 Kato, M. 946
 Kato, R. 81,186,642
 Kato, S. 1258,2488
 Kato, T. 946
 Katsnel'son, B. A. 736
 Katsuta, H. 613
 Katz, C. 237,419,1784
 Katz, J. L. 1412
 Kauffman, C. 2331
 Kaul, B. L. 1399
 Kaump, D. H. 1830
 Kawakami, H. 2170
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 Kawase, A. 20
 Kawashima, K. 946
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 Kawecka-Jaszcz, K. 1272
 Kaweck, K. 1132
 Kay, H. E. M. 2641
 Kayabali, I. 1458
 Keast, D. 1199,1200
 Kedar, E. 2062
 Keeling, J. 2105
 Keith, L. 2136
 Kelada, F. S. 1099
 Kelisky, R. P. 1387
 Kellen, J. 344
 Keller, A. Z. 1384,1663,2530
 Keller, C. A. 534
 Keller, G. H. M. 2278
 Keller, H.-P. 834,1261
 Kelley, N. R. 1449
 Kelley, T. F. 1170
 Kellner, G. 211
 Kelloff, G. 802,814
 Kelly, M. G. 62,252
 Kelly, R. E. 929
 Kendrey, G. 629
 Kennedy, J. R. 1483
 Kenzy, S. G. 507,1618
 Kern, J. 484,2588
 Kerr, H. A. 347
 Kersting, G. 634
 Kerzner, M. S. 1408
 Kessler, I. I. 541,2519,2586
 Kesterson, J. W. 2649
 Ketcham, A. S. 2658
 Ketterer, B. 1777
 Kew, M. C. 202
 Key, C. R. 930,1029
 Keybets, M. J. H. 2278
 Khan, F. M. 940
 Khan, M. H. 2637
 Khazov, P. D. 2158
 Khera, K. S. 403
 Khesina, A. Ia. 2202,2211,2219
 Khitsenko, I. I. 1778
 Khoo, S. K. 1431
 Khoury, G. 120
 Khristov, K. 2257
 Khundanova, L. L. 1180

- Kieff, E. D. 511
 Kiehn, W. K. 617
 Kieker, J. 553
 Kikuchi, Y. 1046
 Kim, C. S. 457
 Kim, U. 394,1405
 Kim, Y. S. 1890
 Kimoto, K. 1140
 Kimura, I. 88,2187
 Kimura, S. 1259,1262
 Kimura, T. 2403
 King, A. M. Q. 1112
 King, C. M. 1853
 King, G. S. 2491
 King, N. W. 513,2040,
 2042
 King, R. J. B. 1523
 King, S. 2316
 King, V. P. 1229
 Kinoshita, R. 1561
 Kinzel, V. 47,1532
 Kipp, W. H. 63
 Kirchhoff, H. 1479
 Kirkland, I. S. 1685
 Kirkland, J. A. 1396,2611
 Kirkman, H. 1130,1833
 Kirkpatrick, D. 1330
 Kirkpatrick, R. 1330
 Kirkwood, J. M. 2489
 Kirn, A. 2498
 Kirsten, W. H. 107,753,
 1566
 Kiriya, B. G. 509
 Kiselev, L. L. 1729
 Kisuile, A. 2609
 Kit, S. 315,852,1278,
 1279,1288,2030,2434,
 2435,2452
 Kitabatake, T. 18,561,
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 Kitamura, I. 518
 Kitchin, D. A. 1092
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 Kjaasen, D. J. 1377
 Kjauber, E. 2259
 Kjaus, S. N. 2671
 Kjaeman, W. 988
 Kjaehues, P. 630,635,
 1191,1518
 Klein, E. 11,108,438
 Klein, G. 300,301,509,
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 945,1617,2039
 Klein, M. 31,2249
 Kleinschmidt, A. K. 2059,
 2465
 Klement, V. 440,458
 Klink, K. 334
 Klug, H. 991
 Kluge, G. W. 2169
 Kluge, E. M. 878
 Klorre, D. 235
 Klose, W. H. 2636
 Klox, B. E. 1934
 Klotzen, T. 1393
 Ko, R.-T. 2567
 Kobayashi, H. 100,764,
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 2597
 Kobayashi, J. 2264
 Kochen, W. 1474
 Kodama, M. 1507,2203
 Kodama, T. 100,764,1507,
 2341,2344
 Kodama, Y. 2205
 Kofman, J. 1044
 Kogan, A. Kh. 2117
 Kogure, K. 1465
 Koh, J. K. 2060
 Koike, N. 946
 Kokavec, M. 1738
 Kolbye, A. C. 166
 Koldovský, P. 279,
 1442
 Kolesnichenko, T. S.
 2290
 Koldziejewska, H. 1375,
 2524
 Kolompár, G. 322,1275
 Komitowski, D. 1134
 Kondi, A. 970
 Kondo, M. 251,422,
 428
 Kondrikov, N. I. 2661
 König, E. 1201
 Konishi, Y. 1156
 Kononova, V. A. 735
 Konrad, P. 547
 Koprowska, I. 2113
 Koprowski, H. 502,1277,
 2441,2470
 Kordač, V. 653
 Korman, V. 1738
 Kornitskii, M. A. 2231
 Korol, W. 93
 Korosteleva, T. A.
 1180,2234
 Korsak, E. 2638
 Korzeniowska, A. 1350
 Koshurnikova, N. A.
 2176,2177
 Koss, L. G. 929,
 1387
 Kosuge, T. 259,744
 Koszarowski, T. 1373,
 2524
 Kothari, M. L. 587
 Kotin, P. 408,1095
 Kourie, F. M. 1650
 Kovács, E. 322,1275
 Kovács, K. 219,375,
 2227
 Koyama, K. 304
 Koyama, T. 1879
 Kozenitzky, I. L.
 1409
 Kozlova, A. V. 1452
 Kozłowski, H. 2668
 Kozuka, S. 1856
 Krajinović, S. 2549
 Král, V. 2207
 Kramarsky, B. 1594,1597,2399
 Krarup, T. 1074
 Krasnitskaia, N. D. 2208,2209
 Krasnow, S. 1343,1647
 Kratzer, F. H. 365
 Krause, W. 1365
 Krawczyk, M. 1350
 Kraybill, H. F. 1014
 Kreider, J. W. 1327,1609,1930
 Kreis, B. 1769
 Kriek, E. 2244
 Krishan, A. 320
 Krishnamurthi, S. 1363
 Krishna Murthy, A. S. 72
 Kritchevsky, D. 314
 Kriukova, I. N. 277,278
 Krivoshapkin, V. G. 2548
 Krivoshein, Iu. S. 2406,2410
 Kroes, R. 720
 Kroh, H. 1051
 Krüger, F. W. 247,1146,1537,
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 Kronman, B. S. 655,656
 Krylova, N. V. 2117
 Kryukova, I. N. 2372
 Kudo, E. 1455
 Kuff, E. L. 1902
 Kühn, B. 169
 Kuhn, W. 488
 Kukain, R. A. 2365
 Kumkumadzhian, V. A. 273
 Kun, M. 336
 Kundel, H. G. 354
 Kung, T. 1307
 Kunte, H. 1785
 Kuntzman, R. 1062,1091,1207
 Kunz, W. 236
 Kunze, E. 244,1536
 Kunze-Mühl, E. 546
 Kupchinskii, L. G. 2375
 Kupfer, G. 249
 Kupfer, M. 249
 Kurahara, C. 106,769,771
 Kurakane, K. 2554
 Kuratsune, M. 1662
 Kurihara, N. 2601
 Kurihara, T. 2198
 Kurimura, T. 315,1278,2434,2452
 Kurita, S. 2605
 Kurita, Y. 88,374,729
 Kurland, L. T. 887,1349
 Kurohara, S. S. 2568
 Kurokawa, S. 561,2168,2604
 Kuroki, T. 230,1863
 Kurstak, E. 516
 Kurtzke, J. F. 1684
 Kutas, J. 358
 Kutinová, L. 1607
 Kutsukača, A. 2170
 Kuwabara, S. 967
 Kuz'min, V. I. 2069
 Kuznetsov, O. K. 1949,2376,2380
 Kuznetsova, N. N. 278,1585,2373
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 Kwan, H. C. 1632
 Kwitten, J. 1401

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 Kyle, J. 1666
 Kyle, R. A. 1349
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 Lacassagne, A. 206,416, 650
 Lafrenz, U. 180,207
 Lafuma, J. 2171
 Lageman, A. 1878
 Lagerlöf, B. 29
 Lahey, M. E. 2104
 Lahiri, V. L. 695
 Laing, D. 825
 Laird, C. W. 1231
 Laird, H. M. 760
 Lake, B. 892
 Laky, R. 358
 Lalich, J. J. 417
 Lamb, E. J. 947
 Lamberson, H. V. 1252
 Lambert, P. M. 2535
 Lambooy, J. P. 1890,1940
 Lamotte, G. 1456
 Lampert, F. 341,2664
 Lampert, P. W. 2496
 Lampson, G. P. 512
 Landmann, R. 2080
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 Lane, M. 2285,2286
 Lane, W. T. 472,814, 1221,1314
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 Lapin, B. A. 2503
 Lappé, M. A. 389,392, 1527,1838
 Lapshin, I. I. 2208
 Laqueur, G. L. 995
 Laron, Z. 2267
 Larsen, W. E. 756
 Larson, E. W. 1581
 Larson, V. M. 840,841, 842
 Lasfargues, E. Y. 822, 1254,1594,1597,2399
 Lasfargues, J. C. 1254, 1597
 Lasne, C. 1070
 Laszlo, J. 140
 Lattimer, J. K. 2044
 Laub, M. 943
 Lauenstein, K. 262
 Laugier, A. 539
 Laurová, L. 550,551
 Lausch, R. N. 1322
 Lavenda, N. 783
 Lavrin, D. H. 1596
 Lavrova, N. A. 2202
 Law, L. W. 755,804, 1980,2015
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 Lawson, T. A. 2253
 Layne, S. 1322
 Lazar, P. 45,1511
 Lazarus, H. 1709,2470
 Lea, A. J. 2133
 Leach, W. B. 2643
 Leader, R. W. 1025
 Leaf, D. S. 1562,2251
 Leahy, M. S. 2266
 Leavell, U. W., Jr. 1417
 Leavesley, G. M. 2625
 Le Bouffant, L. 181
 Lebreuil, G. 1482
 Leclerc, J. C. 762
 Ledin, G., Jr. 1559
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 Lee, A. M. 926,1699
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 Lee, K. P. 309,1269
 Lee, L. F. 511
 Lee, S. S. 1108
 Lee, Y. K. 802,2588
 Leff, J. 2500
 Legrand, E. 361,2151
 Lehman, J. M. 867
 Lehmann, G. 644
 Lehnert, G. 686
 Lehtonen, M. 1380
 Leibman, K. C. 2310
 Leiderman, E. 350
 Leighton, J. 671
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 Lennert, K. 2607
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 Lesko, S. A., Jr. 1088,2206
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 Lespagnol, A. 1082
 Lestchinskaya, N. P. 793,800
 Letourneux, M. 972
 Leuchtenberger, C. 1211
 Leuchtenberger, R. 1211
 Levan, A. 158
 Levenbuk, I. S. 2433
 Levi, P. E. 922,1167
 Levij, I. S. 694,696,1076, 1164,1813,2230
 Levin, M. 2592
 Levin, M. J. 503,2424
 Levin, W. 1062,1207
 Levine, A. J. 2437,2439,2447
 Levine, A. S. 1579
 Levine, E. M. 2470
- Levine, W. G. 2324
 Levinson, W. 795
 Levisohn, R. 2252
 Levy, B. M. 798
 Levy, H. B. 378
 Levy, J. A. 757,1247
 Levy, J. P. 762
 Levy, L. S. 2315
 Lewis, A. C. W. 886
 Lewis, A. M., Jr. 503,2425,2426
 Ley, H. L. 573
 Leymarios, J. 961
 Lhérisson-Straboni, A. M. 496
 Li, C. P. 1310
 Li, E. P. 1225
 Li, F. P. 914,933,1334
 Liban, E. 1409
 Libby, P. R. 1069
 Libermann, C. 45
 Liciu, F. 221
 Liebelt, A. G. 1622,2286
 Liebelt, R. A. 1622,2285,2286
 Lieberman, M. 2333,2334
 Liechty, R. D. 30
 Lief, F. S. 2508
 Lijinsky, W. 66,164,363,1187
 Lilienfeld, A. 2592
 Lillard, H. S. 1105
 Lilly, F. 2336
 Lin, T.-M. 2565,2567
 Lincoln, P. 1063
 Lind, K. 1232
 Lindberg, L. G. 1236,1237,1238
 Lindberg, U. 117,1283,2467
 Linde, H. W. 888
 Lindeman, R. D. 1353,1648
 Lindenfelser, R. 1782
 Lindsay, S. 1433,2132
 Lingeman, C. H. 14,1016
 Linker-Israeli, M. 59,1526
 Links, J. 2394
 Linnik, A. B. 1470
 Linsell, C. A. 970
 Lion, Y. 430
 Lipkovic, P. 2074
 Lipova, V. A. 2209
 Lipschitz, R. 2581
 Lisker, R. 1394
 Liszczak, T. 1614
 Litvinov, N. N. 2280
 Liu, C.-H. 2038
 Liu, G. X. 1108
 Liu, P. I. S. 303,1925
 Ljungberg, O. 948
 Llanos, G. 329
 Llombart, A., Jr. 2259
 Lockhart-Mummery, H. E. 2654
 Loewenstein, W. R. 2111
 Löffler, H. 2443
 Log, T. 449,801
 Loh, P. M. 2308
 Lohs, K. 1720
 Loke, Y. W. 331
 Loktionov, G. M. 2284
 Lombardi, P. S. 2464
 London, W. T. 2591

- Lopes, C. R. N. 1064
 Lopez, A. 1368
 Lora, V. G. 1650
 Louls, C. J. 651
 Loveless, J. D. 1300,2453, 2455
 Lowe, C. R. 1385,2565
 Lowe, D. B. 1764
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 Lowry, J. 1213
 Lucas, R. B. 1419
 Luce, C. F. 2576
 Luciani, J. M. 1716
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 Lucis, R. 1506
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 Lueders, K. K. 1902
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 Lumb, J. R. 2389
 Lundin, F. E., Jr. 2571
 Lunger, P. D. 2495
 Lungu, M. 2371
 Lunts, A. M. 2304
 Luongo, L. 1852
 Luschnitz, E. 834,1261
 Lutcher, F. 619
 Luther, S. W. 1427
 Luthra, U. K. 695
 Lynch, H. T. 15,1742
 Lynch, F. W. 1355
 Lyons, M. 1307
 Lyons, M. J. 2056,2400

 Ma, B. I. 2037
 Maag, T. 1319
 Maamies, T. J. 903
 Maass, H. 1652
 Macek, M. 1607
 Macgregor, A. G. 333
 Macieira-Coelho, A. 456,2099
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 Mack, J. 1479
 Mackay, E. V. 1431
 Mackie, B. S. 691
 MacMahon, B. 335,1356,1385, 2079,2565,2566
 Macpherson, I. 485
 Macpherson, L. W. 2472
 Macpherson, P. 182
 Macrineanu, A. 1750
 MacVaugh, H., III 2160
 Madden, G. E. 678
 Madden, J. W. 2279
 Maeda, K. 2166
 Maeda, M. 774
 Maehara, N. 483
 Mafigiri, J. 2609
 Magee, P. N. 998
 Maggi, V. 2103
 Magnin, F. 1044
 Mahaley, M. S., Jr. 1240
 Maher, V. M. 364,2239
 Mahmoud, I. Y. 783
 Maier, H. G. 1800
 Main, J. H. P. 1274

 Major, I. R. 1188
 Makino, S. 483
 Makino, T. 1455
 Malaise, E. 539
 Malejka-Giganti, D. 3,1540, 2242
 Malendowicz, L. 1111,2295
 Malinin, G. I. 839
 Mallet, L. 600,1093
 Mallet, R. C. 202
 Malling, H. V. 1158,1804
 Mallucci, L. 492
 Malmgren, R. A. 468,815, 1267,1592
 Maltoni, C. 683
 Mamedov, I. M. 2078
 Manaker, R. A. 150,151, 1613,2138
 Mancini, L. O. 124,833
 Mancuso, T. F. 902
 Mandavia, M. 2265
 Mandel, L. R. 1319
 Mandel, M. A. 1197
 Mandelstam, P. 1213
 Mandrik, E. V. 1502
 Manelis, M. E. 2575
 Maniatis, A. K. 156
 Maňka, I. 2259
 Mannering, G. J. 1061,2326
 Mannick, J. A. 2183
 Manning, J. S. 2398
 Manocha, S. L. 923,1054
 Manouvrier, F. 1762
 Mantel, N. 933,1345,1700, 1779,2094
 Maramorosch, K. 321
 Maraud, R. 429
 Marchant, J. 41,42
 Marczyńska, B. 1312,1584
 Marei, A. N. 1453
 Margalith, E. 2027
 Margalith, M. 2026,2027
 Marhold, J. 65,571,648,746
 Mariage, C. 366,367,2292,2293
 Mariani, T. 763,1302
 Marigo, C. 1681
 Mark, J. 112,453
 Marková, H. 911
 Marmol, F. R. 2477
 Marroum-Ghorra, M. C. 136
 Marshak, R. R. 469
 Martel, S. H. 1776
 Martens, J. G. 469
 Martin, D. H. 549,2102
 Martin, H. 25,2637
 Martin, J.-C. 181
 Martin, J. E. 469,538
 Martin, M. A. 501
 Martin, P. 370,371
 Martínez, I. 932
 Martino, E. C. 1310
 Martos, L. M. 2480
 Marty, L. 2031
 Martynova, R. P. 2282
 Maruyama, Y. 940
 Maryak, J. M. 776

 Márza, V. D. 540
 Masera, P. 1446
 Mashekar, B. N. 615
 Maškillejson, A. L. 594
 Massé, H. 2522
 Masse, R. 2171
 Massin, J. P. 1705
 Masubuchi, Y. 1052
 Masuji, H. 1166,1863
 Maternowska, W. 682
 Mathé, G. 266,441,1436,1569, 1574,1977,1982
 Mathison, J. B. 191
 Matos, E. L. 1056
 Maťoška, J. 799
 Matovinovic, J. M. 2266
 Matrka, M. 65,571,648,746
 Matsuhisa, T. 1143
 Matsukura, M. 2340
 Matsumoto, S. 635,1191,1879
 Matsushima, T. 1475,1477,2246
 Matsuya, Y. 2461
 Matsuzaki, M. 2260
 Matte, R. 1402
 Matthes, T. 169
 Matthews, R. S. 599,2218
 Matusuyama, M. 215
 Maujol, L. 328
 Maurer, B. A. 1257
 Maurer, R. 47
 Mauri, C. 1970
 May, E. 853
 Mayer, J. 1773
 Mayer, L. A. 753
 Mazina, N. A. 1789
 Mazurenko, N. P. 2354
 Mazzola, S. 327
 Mazzucco, K. 222,223,224
 McAllister, R. M. 484,485
 McArn, G. E. 153
 McBeath, S. 956
 McBride, R. Z. 1852
 McCarthy, B. J. 1427
 McCollister, S. B. 2312
 McCollough, R. J. 2093
 McCollum, R. W. 1256
 McCombs, R. M. 1616
 McConahey, W. M. 887
 McCormick, K. J. 828,2511
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 McGlashan, N. D. 1122
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 McIntire, K. R. 411,1175

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 McKelvie, D. H. 1034
 McKhann, C. F. 2087
 McKinnell, R. G. 2045,2494
 McLaughlin, B. C. 2021,2411
 McLean, E. P. 415
 McNeill, J. R. 1030
 McNutt, N. S. 986
 McPhedran, P. 917,1678,2593
 McSwain, B. 2555
 Medina, D. 116,286,289,
 710,819,1837
 Medrás, K. 1131
 Meeker, W. R., Jr. 1227
 Meezan, E. 1287,1324
 Mega, T. 2546
 Mehta, F. S. 935
 Mehta, L. A. 587
 Meier, H. 919,1231,1305,
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 Meites, J. 54,1504,1821
 Mekler, L. B. 2384
 Mel, H. C. 2398
 Melamed, M. R. 929,1387
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 Melby, E. C. 1871
 Melchionne, S. 237,419,
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 Meléndez, L. V. 513,2040,
 2041,2042
 Mellière, D. 1705
 Mellors, R. C. 871
 Melnick, J. L. 510,2588
 Melzer, M. S. 612
 Mendez, W. M. 2571
 Meneghelli, P. L. 533
 Menser, M. A. 145
 Menye, P. A. 24,332
 Meranze, D. R. 212,1316,1494,
 1823,1825,1858,1875
 Mercker, P. C. 1898
 Merekalova, Z. I. 1973,2342
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 Merkow, L. P. 61,123,305,
 671,1265,2414,2417
 Merrill, J. A. 906
 Merrington, M. 1677
 Merwin, R. M. 283
 Merz, W. R. 356
 Mestwerdt, W. 1774
 Metcalf, D. 406
 Metchell, E. Z. 85
 Mettler, F. A., Jr. 23
 Meuge, C. 2151
 Meyer, G. 496,856,1273,2466
 Meyer, J. A. 2615
 Meyer, K. K. 1125
 Meyer, R. C. 490
 Meyer-Bertenrath, J. G. 194
 Meyskens, F. 1701
 Meytes, D. 1696,1697
 Michelson-Fiske, S. 454,787
 Mickelsen, O. 240
 Mickey, M. R. 56
 Midtvedt, T. 1489
 Mieler, W. 1026
 Mietkiewski, K. 1111,2295
 Migaki, G. 1691
 Mihoc, M. 540
 Milcu, S.-M. 1750,2181
 Millard, R. E. 2641
 Miller, D. G. 16
 Miller, E. 1101,2368
 Miller, E. C. 672,997,1550,
 1854,2238,2239
 Miller, G. F. 285
 Miller, J. A. 672,997,1439,
 1550,1854,2238,2239
 Miller, J. M. 470
 Miller, L. D. 470
 Miller, R. W. 890,933,1755,
 2137,2518
 Miller, S. V. 736
 Millman, I. 2591
 Miluničová, A. 550,551
 Minaev, A. A. 1481
 Minakami, T. 2264
 Minowada, J. 1257,2631
 Minton, J. P. 864,2058
 Mints, I. M. 1827
 Mintz, B. 159
 Mira, O. J. 2046
 Mirand, A. G. 95,2352
 Mirand, E. A. 95,1227,1626,
 1871,1974,2352
 Miroff, G. 1252
 Mirra, A. P. 2565
 Mirvish, S. S. 58,1529,2221
 Misfeld, J. 174,175,176
 Mishima, Y. 82,968
 Mita, T. 2275
 Mitchell, I. 31
 Mitchell, J. T. 346
 Mitchell, R. E. 2161
 Mitchley, B. C. V. 607
 Mitushin, V. M. 2375
 Mitus, W. J. 156
 Miura, M. 1058,2191
 Miura, T. 2277
 Miyai, T. 1455
 Miyake, S. 2462
 Miyake, T. 2187
 Miyaki, K. 257
 Miyamoto, T. 2385
 Miyata, H. 2166,2597
 Miyata, M. 613
 Miyoshi, I. 260
 Mizell, M. 2489,2490,2491
 Mizuno, K. 353
 Mizutani, S. 2388
 Mizutani, T. 620
 Mlytz, H. 1835
 Möbius, G. 526,527
 Modan, B. 883,1696,1697
 Modovi, B. 976
 Mody, J. K. 1253
 Moertel, C. G. 338
 Mogabgab, W. J. 350
 Mohr, U. 1537,2237
 Mokuno, J. 1676,2600
 Mole, R. H. 168
 Moloney, W. C. 1229
 Mondal, S. 388,2185
 Money, W. L. 2119
 Mongin, M. 1482
 Monjour, L. 366,367,1113,
 2292,2293
 Monnier, J. 734
 Monroe, J. H. 1614
 Montagnier, L. 784
 Montalto, B. 2016,2017
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 Montesano, R. 398,1759
 Montgomery, P. O., Jr. 2276
 Moody, J. A. 64
 Moon, R. C. 57,1212,1826,2327
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 Moore, M. A. S. 406
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 Mordkovich, M. S. 2215
 Moreau, J. 619
 Morehead, R. P. 2660
 Moreo, L. 951
 Morgan, D. L. 2223
 Morgan, H. R. 2387,2464
 Morgan, J. M. 1135
 Morganroth, J. 2432
 Mori, K. 251,422,428
 Mori, M. 2154
 Mori, T. 1501
 Mori, Y. 739
 Moricard, R. 136
 Mori-Chavez, P. 1749
 Morinaga, K. 2554
 Morioka, S. 968
 Moriyama, Y. 2274
 Morozov, K. V. 2382
 Morozzi, G. 603
 Morris, H. P. 1341,1694,1708,
 1858,1904
 Morris, J. E. 417
 Morrison, J. C. 1184
 Morrow, R. H. 509,2609
 Morton, D. L. 285,468,657,815,
 1591,1592
 Morton, J. I. 1580,2048,2332,2347
 Moschetto, Y. 486
 Moscovici, C. 92
 Moskalev, Iu. I. 1746
 Moslander, V. 1687,2552
 Mosse, H. 1206
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 Muggler-Bickel, J. 531
 Mukai, F. 4,1183

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Nosny, Y. 332
Novelli, G. D. 549
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Nowell, P. C. 1003
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Obara, Y. 1402
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O'Brien, R. L. 1066
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 Onoé, T. 256,2154
 Onoka, K. 186
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 Oroszlan, S. 2335
 O'Rourke, J. J. 557
 Orrenius, S. 2204
 Orsi, E. V. 118
 Orth, G. 2473
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 Perraud, R. 2171
 Perry, J. L. 860
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 Peters, J. A. 31,1022
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 Peterson, H.-I. 974
 Peto, R. 22,1098
 Petrova, N. V. 255
 Petrovich, I. K. 1746
 Petrow, Z. D. 1423
 Petrucci, L. 31
 Peydro, A. 2259

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 Rohrbach, R. 1067
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 Rollet, M. 1447

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 Römer, K.-H. 2543
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 Rondia, D. 640
 Rongey, R. W. 2392
 Ronichevskaja, G. M. 2282
 Ronzoni, G. 390
 Ronzoni Bernardi, M. G. 533
 Rose, E. F. 1121
 Rosemond, G. P. 1823
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 Rosenau, W. 950
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 Schaad, R. 2214
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 Schachtschabel, D. O. 1172
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 Schauer, A. 244,1497,1536,2273
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 Scher, W. 1640
 Scherbakova, O. E. 2418
 Scherbaum, O. H. 211
 Schidlovsky, G. 815
 Schiffer, D. 1880,1881,2283
 Schiffer, Z. 916,1391,1392
 Schild, G. C. 2415
 Schilli, W. 34
 Schilling, G. 1091
 Schindler, R. 1007
 Schlee, D. 567
 Schlegel, J. U. 239,423,1100,
 1196,1473,1931
 Schlienger, M. 539
 Schloss, G. T. 617
 Schmähl, D. 247,717,1535,1537
 Schmid, F. A. 49
 Schmidt, C. G. 2037
 Schmidt, R. H. 1150
 Schmutz, J. A. 1814
 Schneider, E. 1690
 Schneider, J. 242,1153
 Schneider, M. 1570,1574
 Schneider, R. 969
 Schneiders, F. 488
 Schnitger, F. 1860
 Schnitzer, B. 340
 Schnohr, P. 2075
 Schnyder, U. W. 2076
 Schochet, S. S., Jr. 2496
 Schoenberg, B. S. 909

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 Schoental, R. 1004,1464
 Schofield, B. H. 1981
 Scholes, V. E. 225
 Scholze, P. 204
 Schön, E. 653
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 Schottenfeld, D. 1359,1665
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 Schrek, R. 2636
 Schulte-Holthausen, H. 2034,
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 Schultz, G. N. 239,423,1931
 Schultze, H. 686
 Schuman, L. 2592
 Schuman, L. M. 2579,2580
 Schütt, M. 1805
 Schütz, C. 1406
 Schwabe, K. 1805
 Schwaier, R. 742
 Schwanitz, G. 1120
 Schwartz, S. O. 2052
 Schwenke, K.-D. 193
 Scott, D. B. M. 347
 Scott, W. 84
 Scriba, M. 2481
 Scribner, J. D. 165,2238
 Scully, R. E. 1403
 Sears, J. F. 877
 Seemayer, G. 1751
 Seemayer, N. 1751
 Segi, M. 2601
 Seidel, H. J. 262,775
 Seidman, H. 1355,1723
 Seidman, I. 1846
 Seif, F. 639
 Seiler, R. 1406
 Seilern-Aspang, F. 222,223,
 224
 Sekely, L. I. 464
 Sekirov, B. A. 2282
 Selim, M. A. 2568
 Seman, G. 294,1600
 Semeraro, D. 519
 Semple, J. C. 1404
 Sen, D. K. 1357
 Sendo, F. 100,764,
 2341,2345
 Senyszyn, J. J. 593
 Sera, Y. 2321
 Serafino, X. 24,332
 Serck-Hanssen, A. 1913,1914
 Sergeev, A. V. 2350
 Sessa, A. 730
 Sevoian, M. 319
 Shabad, L. M. 714,1480,
 2116,2128,2202
 Shaffer, W. L. 906
 Shah, H. H. 1364
 Shahrík, H. A. 413
 Shakhlov, V. A. 2478
 Shamberger, R. J. 1486
 Shanbrom, E. 547
 Shanta, V. 1363
 Shapiro, M. J. 2163
 Shapiro, S. 2564
 Shapiro, S. R. 131
 Sharma, A. K. 1053
 Sharma, J. M. 507,1618
 Sharon, N. 1296
 Shatkin, A. J. 318
 Shaw, G. J. 487
 Shcherbak, N. P. 1086,1787,2213
 Shcherbakova, O. E. 2429
 Shearman, D. J. C. 1045
 Sheehan, W. 2610
 Shein, H. M. 2460
 Shendrikova, I. A. 2208,2209
 Sherman, F. 2106
 Sherry, J. B. 1127
 Sherwood, K. K. 893
 Shevliagin, V. Ia. 1585,2373,
 2375,2384
 Shibuya, C. 2303,2314,2665
 Shikata, E. 321
 Shilo, R. 912
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 Shima, S. 1052
 Shimada, S. 556
 Shimizu, M. 258
 Shimizu, T. 1943
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 Shimojo, H. 304,837
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 Shirai, T. 764,2341
 Shirasu, Y. 620
 Shiratori, O. 267
 Shirley, B. C. 197,1933
 Shirodkar, A. S. 615
 Shisa, H. 1808,1809,1810
 Shiu, G. 461,843,1303
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 Shliankevich, M. A. 2384
 Shoeman, D. W. 1061,2326
 Short, J. G. 2319
 Short, M. D. 1770
 Shubik, P. 421,1022,1759
 Shuklinov, V. A. 2101,2222
 Shultz, G. N. 1100,1473
 Siciliani, M. 1679
 Sidorov, K. K. 2069
 Sidransky, H. 1847
 Siegel, B. V. 1580,2048,
 2332,2347
 Sieger, M. 334
 Siegler, R. 2050,2363
 Sieracki, J. C. 1233
 Sigmon, E. 1209
 Siguenza, R. F. 2480
 Sigurjónsson, J. 2083
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 Sil, R. 1048
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 Šimkovič, D. 284,796,1587
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 Sims, P. 214,379,383,1049,1807
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 Sirsat, S. M. 1055
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 Skinner, E. F. 569
 Škoda, V. 550,551
 Skolyszewski, J. 528
 Skoog, L. 117,2467
 Slack, N. H. 2100
 Sladen, W. J. L. 1239
 Slavin, G. 134
 Slemmer, G. 159
 Slifkin, M. 123,305,671,1265,
 2414,2417
 Slinchak, S. M. 1811
 Słomska, J. 910
 Smart, C. R. 1351,1352,1687,2552
 Smetana, K. 1607
 Smetanin, E. E. 1517
 Smida, J. 113,792,799
 Smidová, V. 113,792,799
 Smirnov, G. A. 1480,2212
 Smirnova, N. E. 2382
 Smith, B. J. 2463
 Smith, C. J. 2225
 Smith, C. K. 2639
 Smith, C. W. 1124
 Smith, E. S. O. 2570
 Smith, F. E. 2285
 Smith, G. 2220
 Smith, G. H. 1599
 Smith, G. V. 1724
 Smith, J. B. 2134
 Smith, J. R. 2313
 Smith, J. W. 90,749
 Smith, J. Y. R. 672
 Smith, L. H. 623
 Smith, M. V. A. 758
 Smith, O. W. 1724
 Smith, P. G. 952
 Smith, R. D. 1202
 Smith, R. E. 92
 Smith, R. R. 666
 Smith, R. W. 2432
 Smith, S. D. 984
 Smolen, V. F. 2186
 Smorodintzev, A. A. 793,800
 Sneider, T. W. 1142,2256
 Snyder, A. L. 1225
 Snyder, D. E. 2186
 Snyder, S. 2504
 Snyder, S. P. 1249,2391
 So, B. T. 638
 Sobczak, E. 848

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 Soehner, R. L. 811
 Soini, A. 2096
 Sokal, J. E. 1405,1460,2635
 Sokol, F. 2057,2442,2451
 Sokova, O. I. 2642
 Soliman, O. 146
 Soll, C. 1365
 Soloimskaia, E. A. 2232
 Solov'ev, Iu. N. 2089
 Somers, K. D. 107
 Somogyi, A. 219,375,2227
 Sorkin, E. 566
 Sorof, S. 1852
 Sorokina, Iu. D. 2224
 Soszka, S. 2624
 Soto, E. 690
 Soubrier, B. 370
 Southam, C. M. 658,1058
 Sóvári, M. 943
 Sowers, J. A. 2322
 Spahn, G. J. 1581
 Spain, D. M. 1163
 Spärck, J. V. 2627,2646
 Spatz, M. 1017
 Spear, P. G. 511
 Speiser, V. 2267
 Spencer, H. C. 2312
 Spicer, C. C. 1677
 Spiers, A. S. D. 1015
 Spiro, R. H. 25
 Spit, P. 133
 Spjut, H. J. 55
 Sprague, R. 2317
 Spratt, J. S. 55
 Sprecher-Goldberger, S. 2589
 Springfield, K. 526,527
 Stachura, J. 682
 Stackpole, C. W. 2490,2492
 Stadler, L. 675
 Staffeldt, E. 2178,2248
 Stahl, A. 1716
 Stamler, F. W. 30
 Stănilă-Oană, L. 1886
 Stanley, M. A. 1396,2611
 Stanley, N. F. 1199
 Stanners, C. P. 861
 Stanton, M. F. 1101,2368
 Stanton, R. 1066
 Stark, C. R. 316
 St-Arneault, G. 1330
 Staroverova, S. 119
 Staszewski, J. 529,542,897,
 1649,2524,2525
 Statnikov, A. M. 2547
 Stavrou, D. 254,636,1519,
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 Stavrovskaia, A. A. 2202
 Stedman, R. L. 1803
 Steele, H. D. 923
 Steele, W. J. 1208
 Steeves, R. A. 1871,1974,
 1975,2338
 Steigrad, S. J. 1367
 Stein, R. J. 417
 Stein, S. C. 127
 Steinberg, A. D. 444
 Steiner, J. 33
 Steinfeld, J. 573
 Steinglass, M. 1006
 Steinhoff, D. 1894
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 Stender, W. 1800
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 Stern, E. 56
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 Stewart, S. E. 85,1255
 Steyn, M. 184,668
 Stich, H. F. 923
 Stier, H. W. 1727
 Stim, T. B. 2049,2337
 Stjernvall, L. 1079,1422
 Stobbe, H. 1423
 Stockert, J. C. 1454
 Stocks, P. 1389
 Stohr, G. 1161
 Stöhrer, G. 618
 Stoian, M. 2371
 Stokinger, H. E. 678,1764
 Stoll, R. 429
 Stoltz, D. R. 403
 Stone, H. M. 1766
 Stookey, J. L. 357
 Strauss, B. 1011
 Strax, P. 2564
 Strel'tsova, V. N. 1746
 Strohl, W. A. 2512
 Strom, R. 976
 Stromberg, K. 1509
 Strömberg, L. E. 1790
 Stromskaia, T. P. 2288
 Strong, E. 25
 Strzelecki, E. 1105
 Stuart, A. 1709
 Stück, B. 2351
 Stuckey, W. J. 350
 Stutman, O. 76,393,431,1198
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 Sugihara, Y. 1756
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 Sugiura, K. 1189
 Sugiyama, T. 374,729
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 Sukacheva, O. A. 2226
 Šula, J. 2207
 Sulitzeanu, D. 2062
 Sumitani, J. 967
 Summers, W. C. 364,2239
 Sunderman, F. W., Jr. 1176,2310
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 Sutnick, A. I. 2591
 Sutton, C. H. 1297
 Sutton, H. 2616
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 Suzuki, K. 946
 Suzuki, S. 2179
 Suzuki, Y. 259,679,774
 Svec, F. 1587
 Svec, J. 796,1587
 Svedmyr, A. 2039
 Sverak, L. 1577
 Svet-Moldavsky, G. J. 2418
 Sviderskaia, T. A. 1744
 Svoboda, D. J. 1179
 Svoboda, J. 786
 Svoboda, V. 881,1376
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 Swain, A. P. 1803
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 Sykes, J. A. 2632
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 Synowiedzka, E. 1350
 Szadkowski, D. 686
 Szakal, A. K. 2349
 Szeder, M. 1348
 Szentivanyi, J. 1742
 Szepsenwol, J. 1493,2328
 Szklanny, J. 336
 Szöke, L. 1348
 Szönyi, F. 1654
 Szulkin, E. 337
 Szwagrzyk, E. 2582
 Szydłowska, H. 2582
 Tabarés, E. 1294
 Tabata, M. 1137
 Tachibana, T. 438
 Taft, P. D. 705
 Taga, N. 1137
 Taguchi, E. 227
 Takada, M. 483,2038
 Takadate, A. 597
 Takagi, N. 317
 Takahashi, A. 642
 Takahashi, H. 29

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 1476,2631
 Takahashi, T. 267,925,2038
 Takaki, R. 425
 Takanaka, A. 81
 Takaoka, T. 613
 Takata, H. 260
 Takatsuki, K. 915
 Takayama, S. 67,192,196,200,
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 Takeda, K. 2141
 Takeichi, N. 100,764
 Takeichi, T. 2341
 Takemoto, K. K. 504
 Takenaka, S. 228,745
 Takeuchi, M. 274,1241,1242
 Takii, M. 425
 Takizawa, K. 98
 Tala, P. 903
 Talal, N. 444
 Talash, M. 2440
 Talbert, J. R. 1127
 Talerman, A. 132,2608
 Talley, R. W. 2553
 Talukder, G. 1053
 Tam, M. R. 2331
 Tamai, A. 243
 Tambourin, P. 99,1568
 Tamplin, A. R. 1748
 Tamura, M. 251,422,428,432
 Tanabe, S. 1258
 Tanaka, T. 1865
 Tandon, P. L. 2573
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 Tanooka, H. 616
 Taper, H. S. 971,1424
 Tapp, E. 1133
 Tarba, M. M. 2007
 Tarin, D. 349,2184
 Tarnowski, G. S. 49
 Tarnowski, W. M. 1520
 Tăşcă, C. V. 2516
 Tasserón, J. G. 2221
 Tauschnitz, C. 834,1261
 Tausch, H. 253
 Taylor, A. C. 798
 Taylor, A. T. 1168
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 Taylor, D. O. N. 439,448,
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 Taylor, J. D. 202
 Teyot, J. 1762
 Te, N.-H. 330
 Tedeschi, F. 1234
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 Teeter, A. 2287
 Tegtmeyer, P. 2033
 Teichmann, R. 1488
 Teitz, Y. 2356
 Teiler, M. N. 1161,1189
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 Tenney, V. A. 1411
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 Tephly, T. R. 646
 Teppo, L. 2578
 Terao, K. 257
 Terekhov, P. E. 2098
 Terenius, L. 1505
 Teresky, A. K. 2447
 Terni, M. 863
 Terracini, B. 721
 Tevethia, S. S. 1322,2428
 Thatcher, F. S. 661
 Theilen, G. H. 105,761,
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 Themann, H. 311
 Theologides, A. 941
 Theuring, F. 1372
 Thewlis, B. H. 610
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 Thurzo, V. 284,1587
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 Tibemanya, J. 878
 Tiggelbeck, D. 1545
 Tiktin, L. A. 2215,2307
 Tilz, G. P. 313
 Timm, J. 174,175,176
 Timmermans, A. 818
 Timofte, D. 1745
 Ting, C.-C. 2457
 Ting, R. C. 94,804,809,
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 Tipnis, U. V. 1055
 Tissier, M. 600
 Titzschkau, E. 2037
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 Tobin, M. S. 1163
 Tobiška, J. 754
 Todaro, G. J. 8,442,504,
 812,851,1225,1293,1752
 2358,2436
 Todd, D. 2570
 Tol, O. 2394
 Tolot, F. 370,371
 Toman, R. 1432
 Tomassini, N. 2442
 Tomii, S. 2546
 Tominaga, T. 1069
 Tomingas, R. 205,643
 Tomioka, S. 353
 Tompkins, W. A. F. 510,
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 Toni, R. J. 802,2369,2390
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 Torpier, G. 2404
 Torten, J. 1280
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 Tot, F. 2372
 Toth, B. 74,421
 Toto, P. D. 2229
 Tough, I. M. 952
 Tournier, P. 853
 Toury, J. 366,1113
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 Treu-Sarnat, G. 1584
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 Trichopoulos, D. 1356,2079,2565
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 Trummer, M. J. 2541
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 Tsetlin, E. M. 2413,2433
 Ts'o, P. O. P. 1088,2206
 Tsubota, T. 260
 Tsuji, K. 1181
 Tsunooka, H. 1347
 Tsuru, K. 1290
 Tu, S.-M. 925,2038
 Tubiana, M. 539,1441,1693
 Tucek, H. V. 1534
 Tukei, P. M. 509
 Tung, T. C. 740
 Turano, A. 109,279,280,1234
 Turbiner, S. 1072,1073
 Turkington, R. W. 139,2647
 Turner, H. C. 408,472,814,
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 Turner, M. K. 201
 Turner, W. 97,270,2370
 Turusov, V. S. 1020,1815
 Tuyns, A. J. 2082,2514
 Tweedell, K. S. 2493
 Tweedell, K. W. 2045
 Tyndall, R. L. 1775,2349
 Tytell, A. A. 512
 Uchida, S. 2028
 Uchino, H. 2165
 Uchiyama, I. 1137

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 Uehara, N. 78,432
 Uehleke, H. 1000,1440,1860
 Uekama, K. 227,2277
 Uematsu, K. 220
 Uhl, N. 525
 Ujházy, V. 799
 Ulland, B. M. 31
 Ullrich, R. 2088
 Ulmer, W. T. 1117
 Umans, R. S. 1088
 Unakar, N. J. 1467
 Ungar, H. 669
 Upchurch, H. F. 2652
 Upton, A. C. 1459,1749,1754
 Uragoda, C. G. 2081
 Urata, Y. 1052
 Urbanowicz, M. 1111,2295

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 v. Hodenberg, A. 1174,1193
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 Vadlamudi, S. 1993
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 Valerio, M. G. 31
 Valladares, Y. 577,1294
 Valleron, A. J. 1693
 van der Gugten, A. A. 115,
 727,728
 van der Noordaa, J. 120,1282
 Van Der Watt, J. J. 2298
 Van De Vorst, A. 430
 Van Duuren, B. L. 237,419,1001,
 1008,1471,1761,1784
 Vane, F. 2326
 Van Esch, G. J. 720
 Van Frank, R. M. 645
 van Gorp, L. H. M. 772
 Van Griensven, L. 1246
 Van Hoosier, G. L., Jr. 518,1308,
 1315,2412
 van Mullem, P. J. 2501
 Van Persijn Van Meerten, O. H.
 681
 van Walbeek, W. 661
 Varela-Nunez, R. 955
 Varet, B. 762
 Vasil'ev, Iu. M. 2202
 Vasil'eva, N. N. 2022,2305
 Vasquez, C. 2465
 Vass, W. 1220
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 Vendrely, R. 380,1525
 Venet, L. 2564
 Venet, W. 2564
 Venkitasubramanian, T. A. 80

 Vepřek, L. 1577
 Verby, J. E. 887
 Verhofstad, F. 727,728
 Verley, J. M. 291
 Vernes, A. 395
 Verney, E. 1847
 Vernole, B. 990
 Vernon, L. 1965,2390
 Vernon, M. L. 1221
 Veronesi, U. 913
 Verrill, B. 989
 Veskova, T. K. 2383
 Veys, C. A. 927
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 Vidal, O. R. 2108
 Vietti, T. J. 89,2107
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 Vitak, M. J. 1420
 Vitsky, B. 1359
 Vizoso, A. D. 1299
 Vlaeminck, M. N. 1083
 Vogel, C. L. 958,959
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 von Haam, E. 949
 Vonkš, V. 874,1607,1616,2061
 von Kreybig, T. 2129
 von Metzler, A. 2192,2193,2194
 Von Niederhäusern, F. 356
 von Studnitz, W. 948
 Vorbrodt, A. 502
 Voronin, E. S. 2382
 Vorvik, D. 2201
 Vredevoe, D. L. 102
 Vulcan, P. 1743
 Vysheslavova, M. Ia. 1842

 Waddell, A. D. 2060
 Waggoner, D. E. 1342
 Wagner, B. P. 1858
 Wagner, J. 1209
 Wagner, J. C. 183,1340
 Wagner, W. D. 678
 Wahi, P. N. 695
 Wahlqvist, L. 2545
 Wakabayashi, A. 788,1435
 Wakabayashi, T. 1027
 Wakisaka, G. 2167
 Wakonig-Vaartaja, T. 1722
 Walburg, H. E., Jr. 589

 Wales, J. H. 362,2330
 Walford, R. L. 547
 Walker, D. L. 2475,2476
 Walker, G. 1868
 Walker, J. L. 2480
 Walker, K. 2319
 Walker, R. 323,324
 Wallace, J. 2489
 Wallace, J. D. 2612
 Waller, R. E. 2537
 Walrond, E. R. 2622
 Wang, C.-H. 2038
 Ward, J. M. 1964
 Warda, B. 2524,2623
 Warner, N. L. 406
 Warrell, D. A. 737
 Warren, S. 1758,2131
 Warzok, R. 253,631,1153,1877
 Watanabe, K. 2180
 Watanabe, M. 1904
 Watanabe, S. 2028
 Watelet, F. 360
 Watler, D. C. 884
 Watne, A. L. 1354
 Watrach, A. M. 310,490
 Watson, J. 1988
 Watson, K. F. 1230
 Wattenberg, L. W. 404,2329
 Waubke, R. 2481
 Webb, M. 51
 Webb, S. J. 2648
 Weber, K. H. 174,175,176
 Wechsler, W. 635,1191
 Wedderburn, N. 1216,1960
 Wei, R. D. 1108
 Weil, C. S. 2130
 Weil, R. 493,495,2144
 Weinberg, A. 831
 Weiner, H. 1412
 Weinstein, I. B. 1538,1929,2243,
 2245,2250
 Weinstein, R. S. 986
 Weir, J. M. 1337
 Weisburger, E. K. 433,434,2249
 Weisburger, J. H. 433,434,1499,
 2246,2249
 Weiss, D. W. 820,821,2053
 Weiss, E. 282
 Weiss, R. A. 1946,1947
 Weissmann, C. 794
 Wellings, S. R. 153
 Wells, G. A. 2480
 Welsch, C. W. 54,1504
 Wender, S. H. 1124
 Wendling, F. 99,1568
 Wepsic, H. P. 2633
 Wepsic, H. T. 654,655
 Werder, A. A. 756,2046
 Werner, U. 1117
 Werthamer, S. 1192
 Westfall, B. B. 345
 Wetteland, P. 1686
 Wever, G. H. 2435
 Whang, J. J. 85
 Whang-Peng, J. 654,1393,2633
 Wheatley, D. N. 214

- heelock, E. F. 1321,1971
 hite, M. R. 1839
 hitehead, J. K. 177,689,1097
 hitescarver, J. 2632
 hittle, E. D. 1157
 HO Expert Committee on Early
 Detection of Cancer: 1445
 lcker, R. 848,849
 idmark, G. 1790
 ieczorkiewicz, A. 535,2524,2525
 ieder, R. 410,1494
 iener, M. 2062
 iese, W. H. 503,2420,
 2426
 iessler, M. 1146,1868
 ijesundera, S. 670,1109
 ildanger, F. 1497,2273
 ilentz, J. M. 2162
 iley, M. 365
 ilhelm, G. 644
 illiams, A. O. 1667
 illiams, D. J. 1115
 illiams, E. H. 133,885
 illiams, G. 1110
 illiams, R. E. 922
 illiams, T. L. 645
 illiams, W. C. 1600,1984
 illiamson, M. E. 513,2042
 ilson, H. 2653
 ilson, W. D. C. 1765
 inkelmann, W. 1799
 inker, J. 685
 inocour, E. 1280,2018
 isniewski, L. 2638
 isseman, C. L., III 1420
 itkowski, F. 535
 itter, R. L. 2149,2486
 ittkop, J. A. 1496
 itz, I. 770
 ivel, N. 1220
 ladron, C. A. 1926
 ogan, G. N. 190,1920,1937
 old, J. W. 1208
 olfe, G. 1249
 olfe, L. 2504
 olff, G. L. 2618,2619,2620
 olff, S. M. 1407
 olfová, H. 911
 ollmann, R. L. 1566
 ombolt, L. 1759
 od, D. A. 285
 od, J. L. 1184
 od, M. 724,1850
 od, P. C. 820,821
 odard, G. 2249
 odliff, H. J. 2625
 odruff, M. 623
 ods, D. A. 697,2225
 ods, M. W. 347
 odside, N. J. 1990
 olner, L. B. 887
 olum, J. C. 1848
 osley, E. T. 1830
 orld Health Organization 2513,
 2517
 ortham, J. S. 46
 Wright, B. S. 93
 Wright, E. A. 234
 Wright, J. K. 22
 Wu, H. 1324
 Wu, H. C. 1287
 Wuest, H. 1058
 Wunderlich, V. 1805
 Wyatt, A. P. 1410,2103
 Wychulis, A. R. 2670
 Wynder, E. L. 35,582,
 931,1513
 Wyse, E. P. 143
 Yamada, K. 1676
 Yamada, S. 1508
 Yamagiwa, H. 939
 Yamaguchi, J. 830
 Yamaguchi, N. 274
 Yamamoto, K. 297
 Yamamoto, N. 1490
 Yamamoto, R. S. 1499
 Yamamoto, S. 620
 Yamamoto, T. 274,1027,
 1241,1242
 Yamane, Y. 1137,2260
 Yamasaki, M. 2168
 Yamasaki, T. 20
 Yamashita, T. 837
 Yamazaki, N. 2170
 Yanagi, S. 1468
 Yancey, S. T. 252
 Yang, C.-S. 2038
 Yang, J. 110
 Yang, M. G. 240
 Yang, W.-K. 549
 Yaniv, A. 979
 Yankee, R. A. 2591
 Yarnell, M. M. 147,148
 Yata, J. 301,1617
 Yates, V. J. 124,833
 Yatoimi, K. 946
 Ydrach, A. A. 1129
 Yeager, G. H. 2306
 Yip, L. C. 1035
 Yohn, D. S. 122,2408,
 2416,2477
 Yokoro, K. 20,2355
 Yokoshima, T. 1151
 Yokota, M. 744
 Yoneyama, T. 588
 Yoshida, K. 243
 Yoshida, M. 2277
 Yoshida, N. 1259,1262
 Yoshida, O. 1780
 Yoshida, T. 659,2038,2546
 Yoshida, T. H. 1863
 Yoshida, T. O. 302
 Yoshiike, K. 1289
 Yoshikawa-Fukada, M. 455
 Yoshikura, H. 268,2366
 Yoshinaga, H. 2172
 Yost, Y. 2251
 Youn, J. K. 149
 Young, B. G. 86,1615
 Young, E. E. 144
 Young, E. M. 1852
 Young, J. C. 776
 Young, L. 710,2053
 Yuasa, S. 2565,2566
 Yuda, K. 2170
 Yule, R. 989
 Yunis, E. J. 431,1198
 Yuspa, S. H. 2223
 Zabezhinskii, M. A. 1883,2233,2272
 Zacharia, T. P. 319,790
 Zackheim, H. S. 2197
 Zadi, Z. 2431
 Zador, S. 1521
 Zajac, B. A. 2481
 Zajdela, F. 99,1568
 Zaki, G. F. 941
 Zaldívar, R. 1899
 Zamfiresco, M. 854
 Zanoio, L. 1798
 Zaritsky, A. 1942
 Zasyanka, A. T. 5
 Závada, J. 780
 Zavadová, H. 874,1607
 Zavala, C. 1394
 Zavanella, T. 628
 Zavodova, T. I. 2440
 Zawirska, B. 1131
 Zayid, I. 543
 Zbar, B. 654,655,2588,2633
 Zedeck, M. S. 1924
 Zeigel, R. F. 471,758,829,2497
 Zeilmaker, G. H. 114
 Zembala, M. 2013
 Zenda, H. 259,744
 Zetterlund, C. G. 1123
 Zeve, V. 1293
 Zharova, E. I. 2354
 Zhavoronkov, A. A. 2478
 Zheleznov, B. I. 2661
 Zhuravleva, T. B. 2120
 Ziegler, J. L. 509
 Zijlstra, U. L. J. 1024
 Zil'fian, V. N. 273
 Zilliken, F. 1172
 Zimel, H. 1750
 Zimmerman, H. M. 992,1297
 Zimmerman, J. 2512
 Zintzsch, I. 249
 Zironi, A. 563,564
 Zisman, B. 875,876
 Ziter, F. A. 2104
 Zobl, H. 866
 Zolotareva, T. M. 2304
 Zóltowska, A. 2668
 Zorini, A. O. 1159
 Zotikov, L. A. 726
 Zschoch, H. 526,527
 Zsigmond, M. 1123
 Zuccari, F. M. 326
 Zuelzer, W. W. 918
 Zülch, K. J. 635,1191,1736
 zur Hausen, H. 2034,2057,2479

ABNORMALITIES, CONGENITAL

- association with malignant tumors, children: 2105, 2137
- chromosomal, leukemia epidemiology, review: 1733
- dermatoglyphic, leukemia, Poland (Cracow): 916
- retinoblastoma: 2108
- epidemiology, leukemia clustering, Wisconsin (Green Bay), children: 2093
- pseudohermaphroditism, hypertension and renal degeneration, with Wilms' tumor, children (2 cases): 2106

ABNORMALITIES, DRUG-INDUCED (See Teratogenesis)

ABSORPTION

- benzpyrene, lung, hamster: 675
- dimethylbenzanthracene, lung, hamster: 675

ABSORPTION, INTESTINAL

- dimethylbenzanthracene, rat: 2327
- polycyclic aromatic hydrocarbons, mechanism, animal: 1213

ABSORPTION, SKIN

- dimethylbenzanthracene, mouse: 1815

ACENAPHTHENE, 5-AMINO-

- leukemia/lymphoma (rat) or bladder tumors (mouse): 1772

ACENAPHTHENE, 5-NITRO-

- leukemia/lymphoma or mammary and bladder tumors, mouse: 1772

ACETAMIDE, N-ACETOXY-N-ARYL-, ESTERS

- nucleophilic substitution, decomposition pathways: 2238

ACETAMIDE, ALLYLISOPROPYL-

- effect on serum hemopexin, rabbit: 1903

ACETAMIDE, N-4-(4'-FLUOROBIPHENYL)-

- liver tumors, age and sex difference, rat: 1509

ACETAMIDE, N-(4-[5-NITRO-2-FURYL]-2-THIAZOLYL)-

- mammary and other tumors, rat: 1510

ACETAMIDE, THIO-

- effect on hormone-induced enzymes, animal: 1933
- hepatoma, rat: 194, 400, 2263
- organ-specific effect on liver glycogen, mouse: 660

ACETONE

- production, intermediate pyrolytic resins, skin tumors and leukemia, animal: 2304

2-ACETYLAMINOFLUORENE (See N-2-Fluorenylacetamide)

ACRIDAN 9,9-DIMETHYL-10-DIMETHYLAMINOPROPYL-, HYDROGEN TARTRATE

- toxicity, mouse: 1840

ACRIDINE

- epidermal hyperplasia, mouse skin: 1188

ACRIDINE, 3,6-BISDIMETHYLAMINO- (acridine orange)

- skin tumors, mouse: 237

ACTIDIONE (See under Antitumor agents)

ACTINOMYCIN D (See under Antitumor agents)

ADHESIVES, SURGICAL

- s.c. tumors, strain differences, mouse: 2306

ADJUVANTS

Freund's

- effect on transplantability of adenovirus 12-induced hamster tumor: 2405

ADJUVANTS (contd.)

- mouse plasmacytoma, leukemia virus-like particles: 1250, 1251

ADRENAL

necrosis

- dimethylbenzanthracene, rat: 209, 214, 375, 1210
- 7-hydroxymethyl-12-methylbenzanthracene, rat: 214

ADRENAL MEDULLA

- calcitonin-like factor, possible pathogenetic significance, multiple endocrine tumor syndrome (Type 2): 2651

ADRENAL NEOPLASMS

- epidemiology, children, Brazil (São Paulo): 1681

- high-occurrence strain of Syrian hamsters: 2097

induction

- lead acetate, rat: 1131
- oral contraceptive, rat: 1830
- ²³⁹Pu, rat: 2177

- pheochromocytoma (epinephrine-producing), with medullary carcinoma of thyroid, familial: 948

ADRENALECTOMY (See under Endocrine ablation)

AFLATOXICOL

- isolation (aflatoxin B1-treated steroid-hydroxylating fungus) and structure: 2297

AFLATOXIN(S)

analysis

- animal feeds: 1918, 2296
- foods of tropical (African) or temperate (French) origin: 2296
- methods: 79, 1917

- bioassay method, amphibian larvae or chick embryo: 1109

biosynthesis

- Aspergillus, cell-free preparations: 80
- culture on tobacco: 748

- effect of refrigeration, Aspergillus flavus: 661

- content, meats: 1104, 1105

- cyclopropenes, toxicity, liver, trout: 665

- dietary, toxicity, farm animals, review: 572

effect on

- blood coagulation, rat: 1107
- connective tissue, rat: 699
- liver, chick embryo: 257
- drug-metabolizing enzymes, animal: 81
- lysosomes, rat liver: 670
- microorganisms, review: 2121
- serum antibodies, mechanism, rat: 367
- environmental, leukemia, Europe, review: 2135
- fluorescent derivatives (from UV-irradiated preparation or biological materials), analysis, method: 664

- food contamination, review: 366

- g.i. tumors, hamster: 187

- induction of serum neoantigen, rat: 2293

- isolation and purification, method: 663

kidney tumors

- hamster: 187
- rat: 362

AFATOXIN(S) (contd.)

liver tumors
 hamster: 187
 rat: 185, 362, 1144, 2292, 2295
 promotion, cycloprobenoid fatty acids,
 trout: 2330
 metabolism, rat, monkey or human: 1113
 teratogenesis, animal: 1859
 toxicity
 chicken: 365, 749
 liver, human: 1914
 monkey: 1913, 2298
 mouse: 1915
 lung, mouse: 701
 species difference, mechanism: 750

AFATOXIN B1
 DNA binding, mechanism: 667, 1919
 effect on
 ameba: 1916
 cholesterol synthesis, rat liver: 186
 dimethylbenzanthracene ovarian tumors,
 mouse: 218
 DNA, RNA and protein, tumor cells: 1106
 fermentation of cellulose, rumen preparation
in vitro: 189
 lysosomes or polysomes, rat liver: 190,
 670
 microsomal benzpyrene hydroxylase, rat
 liver: 1116
 polynucleotides and RNA polymerase, cell-
 free system or rat liver: 1112, 1920,
 1937
 serum proteins, monkey: 62
 excretion, rat: 740
 kidney tumors, rat: 363
 liver tumors
 mouse: 1938
 rat: 188, 363, 1110, 1111, 1938
 salmon or trout, species difference: 666
 trout: 418, 1487
 metabolism
 birds: 2294
 mammals: 184, 668, 1114, 1115, 2294
 steroid-hydroxylating fungi: 662
 mutagenesis and effect on DNA, bacteria: 364
 premalignant liver nodules, in vitro growth
 rate, rat: 671
 synthetic, effect on rat liver: 1937
 toxicity
 rat or mouse: 740, 1938
 skin, rabbit: 669
 species difference, salmon or trout: 666
 transformation product from steroid-hydroxyla-
 ting fungus, structure: 2297
 uptake and liver toxicity, skin painting,
 rat: 1108

LATOXIN B2
 absence of carcinogenic effect, rat: 363
 toxicity, skin, rabbit: 669

LATOXIN G1
 effect on lysosomes, rat liver: 670
 liver and kidney tumors, rat: 363
 toxicity, skin, rabbit: 669

ATOXIN (aflatoxin analog)
 liver, s.c. and intestinal tumors, mouse:
 1488

AGE FACTORS

benzene-induced chromosome abnormalities: 952
 benzpyrene metabolism, liver microsomes, rat:
 643
 breast cancer, international: 1388
 cancer epidemiology
 children and adolescents, U.S.: 890
 Italy (Milan): 2096
 CNS disease induced by transplantable leukemia,
 mouse: 2331
 dimethylbenzanthracene carcinogenesis, rat:
 212, 376
 leukemia, mouse: 220
 familial cancer occurrence: 1679
 fluorobiphenylacetamide hepatoma, rat: 1509
 growth curves, osteosarcoma development: 2089
 herpesvirus resistance, role of macrophages,
 mouse: 876
 host immunity
 adenovirus-12 or SV40 tumors, hamster: 1603
 cancer incidence, review: 1446
 high-plasma cell tumor mouse strain: 973
 hydroxyfluorenylacetamide tumors, rat: 2249
 leukemia epidemiology
 Georgia (Atlanta), ethnic groups: 2593
 Japan: 1674
 review: 1013
 malignant melanoma incidence, U.S.: 2528
 mast cell proliferation, NZB mice: 1706
 methylcholanthrene tumors of lung transplants,
 mouse: 2187
 skin cancer, Germany (Giessen): 1365
 spontaneous remission of Friend viral leukemia,
 mouse: 1630
 streptokinase-induced lymphocyte transformation,
 human: 1702
 tracheobronchial gland development, conventional
 and germ-free mice: 2102

Agrobacterium tumefaciens
 bacteriophage PS-8, plant tumors: 2500

AIR POLLUTION
 automobile exhaust, USSR (rural): 735
 benzpyrene
 aircraft exhaust gases and soot: 1480
 analysis, methods: 1085, 1789, 1790
 automobile exhaust gases, engine efficiency
 and gasoline quality: 1481
 bioassay method (mouse): 1791
 coke plant, USSR: 255
 dust, Switzerland, urban (Zurich) and rural:
 2214
 review: 2116
 dust and gaseous, cancer epidemiology,
 England and Wales: 1660, 1661
 fuel consumption, cancer epidemiology, France:
 2521
 lung cancer
 coal mining and textile-manufacturing
 areas, England and Wales: 1660
 Japan (Amagasaki and Nishinomiya): 2538
 proposed studies of community health: 902
 review: 574
 Scotland, urban and rural: 2536
 smoking, East Germany: 2543
 polynuclear hydrocarbons, analysis, method:
 603, 1786

AIR POLLUTION (contd.)

- radioactive, dosimetry, method: 1753
- respiratory diseases
 - data evaluation methods: 2537
 - Great Britain: 2535, 2536
 - Japan (Tokyo): 1657
- stomach cancer, England and Wales: 1661
- sulfur dioxide, possible effect on arsenic as respiratory carcinogen, human: 1699

ALCOHOL CONSUMPTION

- brain tumors, Minnesota: 2580
- esophagus cancer
 - geographical distribution, France: 2081
 - Jamaica and Western Australia, comparison: 2533
- liver cirrhosis
 - hepatoma, Japan: 2560
 - malignant transformation: 1415

ALCOHOLIC BEVERAGES

- analysis, high-esophagus cancer regions, central Africa (Zambia and Malawi): 1122

ALKYLATING AGENTS (See under Antitumor agents)

ALUMINUM-DEXTRAN

- effect on methylcholanthrene tumors, rat: 2192

AMINES AND AMIDES, AROMATIC

- activation to active carcinogens, mechanism, review: 997
- arylhydroxylamines, oxidation to nitroso derivatives, method: 738
- carcinogenic or noncarcinogenic, free radical formation, organic solvents or water: 598
- DNA photosensitization: 2203
- environmental and occupational exposure, bladder cancer: 1119, 1782
- mechanism of action, review: 3, 1439, 1440
- mutagenesis, bacteria: 2239
- toxicity, mechanism, review: 1000

AMINO ACIDS

- nucleohistones, adenovirus or adenovirus-SV40 hamster tumors: 486

AMINO ACIDS, AROMATIC

- interaction with nitroquinoline oxide, mechanism: 228
- structure-activity relationships, review: 353

AMINOPTERIN (See under Antitumor agents)

ANDROGENS (See also specific compounds)

- effect on adenovirus-12 tumors, hamster: 122
- metabolism
 - breast cancer: 1412
 - review: 1
- women with larynx cancer: 1835

ANEMIA, PERNICIOUS

- stomach cancer, Minnesota (Minneapolis): 2551

ANESTHETICS

- occupational exposure, cancer incidence, U.S. and Canada: 888

ANILINE, DIMETHYL-

- effect on liver microsomes, rat: 2240, 2241

ANISOLE DERIVATIVES

- skin cancer, mechanism, review: 351

ANTHRACENE, 2-AMINO-

- skin tumors, dermal collagen synthesis, rat: 1466

ANTHRACENE, 9-BROMOMETHYL-

- effect on DNA, normal cells: 619

ANTHRANILIC ACID, 3-HYDROXY- (tryptophan metabolite)

- bladder tumors
 - effect of ascorbic acid, mouse: 239, 423, 1931
- hydroxyanthranilic acid distribution, rat: 1474
- effect on urinary cinnabarinic acid formation, bladder cancer: 1196
- excretion, bladder cancer: 1195
- dietary factors, Africa (Uganda): 1368
- related compound, bladder tumors, effect of ascorbic acid, mouse: 1473

ANTIBIOTICS

- chromosomal abnormalities, review: 1716
- rifampicin, effect on Rous sarcoma virus production and transformation, chick embryo cells: 794

ANTICOAGULANTS

- effect on transplanted tumors, mouse: 2302

ANTICONVULSANTS

- hydantoin type, lymphoma, human: 1909, 1910

ANTIDEPRESSANTS

- toxicity, mouse: 1840

ANTILYMPHOCYTE SERUM (See Immune serum)

ANTIMETABOLITES (See under Antitumor agents)

ANTITUMOR AGENTS

- acetylenic carbamate type
 - effect on Friend virus leukemia, mouse: 265
- actinomycin D
 - effect on
 - avian leukosis-sarcoma or fowl plague virus, role of cellular DNA, chick or hamster embryo cells: 780
 - dimethylbenzanthracene carcinogenesis, mouse: 46, 218
 - erythropoiesis, Friend leukemia virus-infected mouse: 1568
 - methylcholanthrene skin tumors, mouse: 2182
 - Moloney sarcoma virus transformation, mouse embryo cells: 803
 - mouse hepatitis-sarcoma virus system *in vitro*: 111
 - polyoma-infected cells: 2014
 - SV40 transplantation antigen (monkey cells) and tumor induction (hamster) 1641
- actinomycin S or actinomycin D
 - s.c. sarcoma, mouse: 1539
- aminopterin
 - effect on liver or spleen tetrahydrofolate dehydrogenase, mouse viral leukemias: 2350
 - mutagenesis and effect on tumor incidence, *Drosophila*: 626
- antibiotics
 - effect on surface antigens, EB virus-positive Burkitt lymphoma cells: 1617
- antimetabolites
 - effect on surface antigens, EB virus-positive Burkitt lymphoma cells: 1617
- asparaginase
 - effect on Rauscher viral leukemia, mouse: 1579

SUBJECT INDEX

ANTITUMOR AGENTS (contd.)

- 5-blis (2-chloroethyl)amino-6-methyluracil
(thymine alkylamine)
effect on Rous sarcoma virus-transformed
rat cells: 796
- bleomycin
effect on nucleus, methylcholanthrene-
induced skin tumor, mouse: 256
- bromodeoxyuridine
effect on
Marek's disease virus, chick or duck
embryo cells: 2487
Rous virus transformation, chick embryo
cells: 2387
- busulfan
effect on WBC chromosomes, polycythemia
vera: 1031, 2641
- complications of therapy, cytomegalovirus
infection, human leukemia: 1612
- cycloheximide
effect on
dimethylbenzanthracene ovarian tumors,
mouse: 218
skin carcinogenesis, mouse: 47
- cyclophosphamide
effect on dimethylbenzanthracene cheek
pouch tumors, hamster: 2230
Moloney viral sarcoma, mouse: 1589, 1635
stimulation of brain tumor, human: 1747
toxicity, liver, mechanism, rat: 1860
- cytosine arabinoside
effect on
Moloney or Rauscher virus in vitro:
272, 1956, 1958
SV40 transplantation antigen (monkey
cells) and tumor induction (hamster):
1641
Yaba poxvirus-infected cells: 2477
- fluorodeoxyuridine
effect on SV40 transplantation antigen
(monkey cells) and tumor induction
(hamster): 1641
- 5-fluorouracil
effect on dimethylbenzanthracene skin
tumor, mouse: 404
- hydroxyurea
effect on 2-stage skin carcinogenesis,
mouse: 1513
- iododeoxyuridine
effect on SV40 transformation, hamster
embryo cells: 846
- liver extract from clam (Mercenaria mercenaria)
effect on adenovirus-12 tumor, hamster:
1310
- 6-mercaptopurine
effect on
Friend leukemia virus infection, mouse:
96
radiation leukemogenesis, mouse: 21
leukemogenesis (cell-free passage of thymic
lymphoma), mouse: 1552, 2389
- methotrexate
effect on dimethylbenzanthracene cheek
pouch tumors, hamster: 2230
- 6-methylmercaptopurine ribonucleoside
effect on polyoma virus, mouse embryo cells:
1625

ANTITUMOR AGENTS (contd.)

- mitomycin C
effect on
liver phospholipids, dimethylamino-
azobenzene hepatoma, rat: 1139
Moloney sarcoma virus transformation,
mouse embryo cells: 803
SV40- or polyoma virus-transformed cells:
2010, 2024
s.c. sarcoma, mouse: 1539
- mutagenic, screening method, mouse: 1555
- nitrogen mustard
lung tumors, mouse: 701
- polyfunctional alkylating agents
teratogenesis, animal: 1859
- ³²P
effect on chromosomes, polycythemia vera:
2641
- procarbazine (ibenzmethylin)
lung or s.c. tumors, animal: 252, 605
- prodigiosan (interferon-stimulating antibiotic)
effect on Friend virus leukemogenesis,
mouse: 2346
- puromycin
effect on mouse hepatitis-mouse sarcoma
virus system in vitro: 111
relationship of teratogenic and carcinogenic
activity, animal, review: 2129
- streptozotocin
mechanism of action, bacteria and tumor
cells: 1155
- synthetic copolymer
effect on viral leukemia, mouse: 97
- TEM
effect on Friend leukemia virus infection,
mouse: 96
- terephthalanilide
effect on Friend leukemia virus infection,
mouse: 96
- toyocamycin
effect on avian myeloblastosis virus in vitro:
1577
- vinblastine
effect on
dimethylbenzanthracene cheek pouch
tumors, hamster: 1813, 2230
skin tumors, resistant mouse strain:
1079
- ANUS NEOPLASMS
epidemiology
Jamaica: 2557
Tennessee (Nashville), ethnic groups: 2555
- APPENDECTOMY (See under Surgery)
- L-ARGININE-L-GLUTAMATE
effect on isoniazid or hydrazine lung tumors,
mouse: 1499
- AROMATIC COMPOUNDS
structure-activity relationships, review: 353
- ARSENIC
mechanism of action, normal human cells: 2311
occupational exposure
chronic toxicity, Poland (Zloty Stok):
1118
respiratory cancer, role of air pollution:
1699
U.S.: 926
skin cancer, human: 1776

ASBESTOS

- asbestos bodies, prevalence, Michigan (Detroit and Lower Peninsula): 1102
- benzpyrene-adsorbed, effect on benzpyrene uptake by lung, hamster: 2201
- biological effects, review: 1713
- contamination by polyethylene containers: 32
- detection
 - asbestosis: 182, 680
 - mesothelioma, method: 181, 412
- environmental exposure, review: 1018
- lung tumors, rat: 1101, 1340
- migration from s.c. inj. sites, mouse: 1103
- occupational exposure
 - bronchial cancer: 1762
 - cancer incidence, New York and New Jersey, review: 2071
 - leukemia/lymphoma, New York: 1763
 - lung cancer, Japan: 2320, 2321
 - mesothelioma: 681, 1482
 - West Germany (Hamburg): 1370
- mesothelioma, rat: 183, 1101, 1340
- structure and development of asbestos bodies, lung, hamster: 679
- trace metals, effect on benzpyrene hydroxylase, mouse lung: 1764

ASCARIDOLE

- effect on DNase-II, cell-free system: 612

ASCORBIC ACID

- effect on
 - bladder tumor induction, mouse: 1473
 - skin carcinogenesis, mouse: 1486
 - tryptophan metabolite bladder carcinogenesis, mouse: 239, 423

Aspergillus fumigatus

- afutoxin, liver, s.c. or intestinal tumors, mouse: 1488

ATHEROSCLEROSIS, CALCIFIED

- association with stomach cancer and ulcer: 2110

AUTOIMMUNE DISEASES (See under Immunity disorders)

AUTOMOBILE EXHAUST (See under Engine exhaust gases)

AZAPROPAZONE (See 1,2,4-Benzotriazine, 3-dimethyl-amino-7-methyl-1,2-(n-propylmalonyl)-1,2-dihydro)

AZATHIOPRINE

- ervical dysplasia, human: 705

AZIRIDINE DERIVATIVES

- lung tumors, bioassay method, mouse: 410

AZO COMPOUNDS, ALIPHATIC

- structure-activity relationships, rat: 1193

AZO DYES

- effect on liver RNA, rat: 201
- tritiated, synthesis: 739

AZOANILINE, N,N-DIMETHYL-P-PHENYL-

- toxicity, insect (cockroach): 624

AZOBENZENE, o-AMINO-

- effect on dimethylaminoazobenzene hepatoma, rat: 659

AZOBENZENE, N-BENZOYLOXY-N-METHYL-4-AMINO-

- mutagenesis, *Drosophila*: 1182

AZOBENZENE, 2,5-DIMETHOXY-4-AMINO-

- toxicity, rat: 1889

AZOBENZENE, 7,12-DIMETHYL-

- liver tumors, liver glycogen, rat: 1549

AZOBENZENE, 4-DIMETHYLAMINO-

- derivatives, structure-activity relationship, rat: 63, 197, 1860, 1890

effect on

- liver enzymes, rat: 2260, 2261, 2262, 2263
- normal, transformed or neoplastic rat or mouse cells: 613

- WBC phagocytic activity, rat: 1180

liver tumors

- mouse: 1467

- rat: 192, 198, 203, 206, 416, 430, 650, 659, 920, 1137, 1138, 1139, 1140, 1495, 1885, 1886, 1940, 2154, 2258, 2259, 2261, 2262, 2263, 2264

- metabolism, bile, rat: 65, 648

AZOBENZENE, N,N-DIMETHYL-4-AMINO-

- oxidation, cerium(IV) sulfate: 746

AZOBENZENE, 4'-FLUORO-4-DIMETHYLAMINO-

- hepatoma, nuclear RNA, rat: 396

AZOBENZENE, 3-METHOXY-4-AMINO-

- liver tumors, rat: 1889

AZOBENZENE, 2-METHYL-4-DIMETHYLAMINO-

- liver tumors, rat: 1887

AZOBENZENE, 3'-METHYL-4-DIMETHYLAMINO-

- binding, mechanism, rat liver proteins: 1777

- effect on RNA or DNA, rat liver: 2255, 2256

- serum proteins, monkey: 62

- WBC phagocytic activity, rat: 1180

liver tumors

- guinea pig: 199

- rat: 395, 396, 651, 652, 1141, 1142, 1143, 1468, 1847, 1887, 1888, 1891, 1893, 2154, 2179, 2180

AZOBENZENE, 4'-METHYL-4-DIMETHYLAMINO-

- liver tumors, nucleolar RNA composition, rat: 1143

AZOBENZENE DERIVATIVES

- structure-activity relationships, review: 571

AZOTOLUENE, o-AMINO-

- effect on liver and serum proteins, mouse: 2234

liver tumors

- mouse: 1169, 1895

- trout: 418

AZOXYMETHANOL, METHYL- (See Cycasin aglycone)

AZULENO(5,6,7-cd)PHENALENE

- s.c. sarcoma, mouse: 1546

BACTERIA

- anaerobic, benzpyrene synthesis

- culture media: 601

- soil samples: 600

- carcinogen production, review: 162, 163

effect of

- aflatoxins, review: 2121

- β -propiolactone: 1490

BACTERIOPHAGE

- Agrobacterium tumefaciens*, plant tumors: 2500

- DNA, effect of β -propiolactone: 1490

- mutagenesis, nitroquinoline oxide: 1862

BENZ(c)ACRIDINE, 7,10-DIMETHYL-

- effect on crustacean eggs: 1861

ENZANTHRACENE

effect on

dimethylbenzanthracene cytotoxicity,
hamster embryonic cells: 36DNA, rat mammary gland, hormone effects:
1523

,2-BENZANTHRACENE

analysis, petrochemical effluents, method:
1827effect on microsomal enzymes, mechanism,
hamster cells: 1828

epidermal hyperplasia, mouse skin: 1188

metabolism, effect of α -naphthoflavone, normal
cells: 409photodynamic effect, Neurospora or hamster
cells: 1804skin tumors, cocarcinogen effects on threshold
response, mouse: 1087

BENZANTHRACENE (benz[a]anthracene)

effect on enzymes, hamster embryo cells: 647

skin tumors, mouse: 1784

transformed cells, benzpyrene cytotoxicity:
381

tumor induction, planaria: 627

NZANTHRACENE, 7-BROMOMETHYL-

effect on DNA, normal cells: 619

metabolism, mouse embryo cell cultures: 383

NZANTHRACENE, 7-BROMOMETHYL-12-METHYL-

mutagenesis, Drosophila: 1182

NZANTHRACENE, 1,2:3,4-DI-

effect on proteins, mouse skin: 2221

epidermal hyperplasia, mouse skin: 1188

NZANTHRACENE, 1:2,5:6-DI-

binding, skin proteins, mouse: 698, 2221

effect on Rous virus tumors, chick: 52

epidermal hyperplasia, mouse skin: 1188

mechanism of action, review: 2155

photodynamic effect, Neurospora or hamster
cells: 1804

skin tumors, mouse: 384, 1784

NZANTHRACENE, 1:2,7:8-DI-

epidermal hyperplasia, mouse skin: 1188

NZ(a,h)ANTHRACENE, DI-

metabolism, mouse embryo cells: 2219

NZ(a,h)ANTHRACENE, DI-, 5,6-OXIDE

metabolism, rat liver enzyme: 379

NZANTHRACENE, 7,12-DIMETHYL-

adrenal necrosis, rat: 209, 214, 375, 1210

brain tumors, rat: 1819

carcinogenic effect, hamster strain (Phodopus
sungorus): 2642cervix tumors, effect of contraceptives, mouse:
1128cheek pouch tumors, hamster: 373, 694, 695,
696, 697, 1075, 1076, 1926, 2225, 2229,
2230cytotoxicity, effect of other carcinogens,
normal cells: 36, 409

effect on

chromosomes, leukemic or preleukemic rat
bone marrow: 729

cutaneous nerves, mouse or rabbit: 1818

differentiation, rat muscle cultures: 2222

DNA, mechanism, normal cells: 36, 1204, 2223

rat mammary gland, hormone effects:

1069, 1523

BENZANTHRACENE, 7,12-DIMETHYL- (contd.)

Friend virus leukemia, mouse: 617

LDH isoenzymes, human fibroblasts: 211
ovarian gonadotropin response, mouse or
rat: 216

RNA, mouse skin: 1525

Rous virus tumors, chick: 52

virus-free preneoplastic mammary outgrowths,
mouse: 1836

epidermal hyperplasia, mouse skin: 1188

tumors, oophorectomized rat: 44

hepatoma

effect of dimethylaminoazobenzene, rat: 650

germ-free mice: 611, 702

immunosuppression, newborn or adult mouse:
614kidney tumors, rat, effect of oophorectomy:
1820

leukemia

mouse: 220, 1808, 1809, 1810, 1811

rat: 374

lung tumors, mouse: 702, 703, 1039

lymphoma

hamster: 74

mouse: 210, 377, 731, 2389

mammary tumors

mouse: 210, 649, 1253, 1811

rat: 44, 54, 56, 57, 212, 219, 376, 708,
709, 711, 920, 938, 1041, 1070, 1071,
1558, 1821, 1823, 1824, 1825, 1898,
2226, 2227, 2228

virus-like particles: 1598, 2000

metabolism

animal: 675, 1212, 1213, 1520, 1815,
1826, 2327

mammalian cells: 383, 2202, 2219, 2220

mutagenesis, Drosophila: 382, 1182

nucleic acid and protein binding, rat or

mouse tissues or tumor cells: 47, 1524,
1801, 1805

osteosarcoma, hormone effects, rabbit: 2231

ovary tumors, mouse: 210, 217, 218, 649,
1074, 1522photodynamic effect, Neurospora or hamster
cells: 1804

respiratory tumors, hamster: 207

salivary gland tumors, rat: 1072, 1073,
1812, 1814sarcoma, s.c. graft of gastric cyst, mouse:
215

s.c. tumors

hamster: 1816

mouse: 49, 611

primate: 50

rat: 2264

skin tumors, mouse: 35, 45, 46, 47, 208,
237, 378, 404, 1067, 1077, 1078, 1079,
1486, 1513, 1521, 1784, 1803, 1815, 1817,
2157soluble tumor antigens, delayed hypersensitivity
reaction, guinea pig: 415

structure-activity relationship, proton

magnetic resonance spectra: 2218

teratogenesis, rat: 1807

thymoma, mouse: 76, 1198

thyroiditis, rat: 213

- BENZANTHRACENE, 7,12-DIMETHYL- (contd.)
 transplacental
 embryotoxicity, mouse: 2224
 review: 2128
 lung or kidney tumors, mouse: 714
 skin tumors, mouse: 2329
- BENZANTHRACENE, 7-HYDROXYMETHYL-
 teratogenesis, rat: 1807
- BENZANTHRACENE, 7-HYDROXYMETHYL-12-METHYL-
 adrenal necrosis, rat: 214
 teratogenesis, rat: 1807
- BENZANTHRACENE, 12-HYDROXYMETHYL-7-METHYL-
 teratogenesis, rat: 1807
- BENZANTHRACENE, 7-METHYL-
 metabolism, mouse embryo cells: 383
- 1,2-BENZANTHRACENE, 6,9,10-TRIMETHYL-
 brain tumors, DNA and histone content and
 chromosomes, rat: 632
- BENZANTHRACENE, 7,8,12-TRIMETHYL-
 leukemia and mammary tumors, rat: 1829
- BENZANTHRENE DERIVATIVES
 cysteine conjugates, effect on aminoacyl-RNA
 synthetase, cell-free system: 1184
 metabolism, effect of methylcholanthrene,
 rat liver microsomes: 1049
 ovary tumors, structure-activity relationship,
 mouse: 1522
 skin tumors, structure-activity relationship,
 mouse: 1187
 transformation, hamster embryo cells,
 structure-activity relationship: 1553
- BENZENE AND BENZENE DERIVATIVES
 occupational exposure, leukemia: 369, 370,
 371, 372, 951, 952, 1120
- BENZENE, DODECYL-
 toxicity, lung, mouse: 701
- BENZENE, HEXAMETHYL-
 skin tumors, mouse: 1478
- BENZENESULFONATE, ALKYL-
 g.i. tumor promotion, rat: 1476
- 11,12-BENZFLUORANTHENE
 toxicity, mouse: 2237
- BENZFLUORANTHENE, 3:4,10:11,12:13-TRI-
 toxicity, mouse: 2237
- BENZIDINE
 aerosol, mammary tumors or leukemia, rat: 2233
 occupational exposure, bladder cancer, U.S.:
 545
 poisoning, rat: 2232
- BENZIDINE, N,N'-DIACETYL-
 poisoning, rat: 2232
- BENZIDINE 3,3'-DICHLORO-
 poisoning, rat: 2232
 transplacental, effect on embryonic kidney or
 lung, mouse: 714, 2128
- BENZIDINE, 3,3'-DIHYDROXY-
 poisoning, mechanism, rat: 2232
- 3,3'-BENZIDINEDICARBOXYLIC ACID
 leukemia and lung or liver tumors, rat: 1923
- BENZOFURAN, 3-AMINODI-
 bladder tumors, mouse: 2253
- BENZO(rst)PENTAPHENE (See Benzpyrene, 3:4,9:10-di-)
- BENZO(ghi)PERYLENE
 analysis, medicinal wax (ozokerite ceresin)
 from USSR: 2307
 metabolism, mouse embryo cells: 2219
 skin tumors, mouse: 1784
- BENZO(a)PYRENE (See 3,4-Benzpyrene)
- BENZO(e)PYRENE
 metabolism, mouse embryo cell cultures: 383
- 1,2,4-BENZOTRIAZINE, 3-DIMETHYLAMINO-7-METHYL-
 1,2-(n-PROPYLMALONYL)-
 toxicity, mouse: 1840
- BENZOTRIAZOLE
 toxicity, rat or mouse: 2305
- 1,2-BENZPERYLENE
 analysis, coffee substitutes: 1800
- 1,2-BENZPYRENE
 effect on RNA, mouse skin: 1525
- 2-BENZPYRENE
 photodynamic effect, *Neurospora* or hamster
 cells: 1804
- 3,4-BENZPYRENE
 abnormal cellular responses, insect (cockroach):
 625
 air pollution
 analysis, methods: 1085, 1789, 1790
 bioassay method (mouse): 1791
 coke plant, USSR: 255
 analysis
 air-borne dust, Switzerland, urban (Zurich)
 and rural: 2214
 coffee substitutes: 1800
 meat and milk from benzpyrene-fed cows:
 2216
 medicinal wax (ozokerite ceresin) from
 USSR: 2307
 petroleum refining products: 2211
 prunes, processing methods: 2215
 salt, processing methods: 2210
 smoked fish, processing methods: 2208, 2209
 soil and plants: 1086, 1787, 1792, 2212
 attempted s.c. tumor induction, cattle: 1068
 biosynthesis, bacteria: 600, 601, 1093
 brain tumors, rat: 234, 1094
 cervical atypia, radiation effects, mouse:
 1036
 chlorinated derivatives, toxicity, mouse:
 602
 cytotoxicity
 effect of α -naphthoflavone, normal cells:
 409
 normal or transformed animal or human cells:
 381
 diagnostic use, ruptured placental membranes,
 human: 1798
 diesel oil containing, yeast culture medium,
 hydrocarbon biosynthesis: 2207
 dietary, stomach cancer, Iceland: 2083
 distribution and metabolism
 animal: 34, 641, 675, 1095, 1213, 1528,
 1794, 1799, 2201, 2216, 2217, 2324
 human: 1796
 DNA binding, mechanism: 1066, 1088, 2206
 effect on
 immunity, mouse: 614
 liver microsomes, rat or hamster: 180,
 205, 643, 646, 1090, 1091, 1116, 1797,
 2204, 2324
 metabolism of other polycyclic hydrocarbons,
 rat liver: 640
 RNA, mouse skin: 380, 1525
 Rous virus tumors, chick: 52
 environmental, review: 2116

- 4-BENZOPYRENE (contd.)
 exhaust gases
 aircraft engines of different types: 1480
 automobiles, gasoline quality and engine efficiency: 1481
 g.i. tumors, rat: 241
 hair follicle tumors, growth rate, mouse: 920
 hydroxylase
 effect of trace metals and asbestos, mouse lung: 1764
 liver, strain differences, mice: 2205
 methylcholanthrene induction, rat liver or hepatoma: 1904
 leukemia, strain differences, mouse: 1479
 lung tumors
 hamster: 1089
 mouse: 2199
 rat: 1793
 mechanism of action, theoretical model: 1084
 metabolism, mammalian cells: 383, 1551, 2202, 2219
 nucleic acid and protein binding, mouse or rat tissues: 47, 1524
 osteosarcoma, rat: 2198, 2200
 photodynamic effect, *Neurospora* or hamster cells: 1804
 reaction with imidazoles, DNA and RNA, mechanism: 387
 s.c. tumors
 effect of adenovirus, hamster: 303
 primate: 50
 skin tumors, mouse: 1078, 1087, 1486, 2237
 soil extracts containing, skin tumors, mouse: 2213
 solid tumors, chromosomes, rat: 1053
 solubilization, role of deoxyadenosine monophosphate-silver ion complex: 747
 squamous metaplasia of trachea, effect of citral or vitamin A in vitro, hamster: 1795
 stomach tumors
 hamster: 1089
 mouse: 2315
 structure-activity relationship, proton magnetic resonance spectra: 2218
 tobacco smoke component, lung tumors, mouse: 1768
 transformed hamster cells
 cytotoxicity of other carcinogens: 401
 hamster tumors: 385
 transplacental, lung tumors, mouse: 2329
 transplantable mouse sarcoma, effect of guinea pig RNA: 1059
 tumor induction, planaria: 627
 tumor regression by adenovirus 12-infected or transformed cells, hamster: 1925
 water pollution, method of removal: 1788
 NZPYRENE, 3:4,9:10-DI-
 distribution, mouse: 1170
 s.c. tumors, prevention by essential oils, mouse: 1214
 skin tumors, accelerated induction method, mouse: 384
 NZPYRENE, 3:4,9:10-DI-, 5-AMINO-
 s.c. sarcoma, mouse: 386
 BENZOPYRENE, 3:4,9:10-DI-, 5-NITRO-
 s.c. sarcoma, mouse: 386
 BENZOPYRENE DERIVATIVES
 metabolism, effect of methylcholanthrene, rat liver microsomes: 1049
 6-substituted, effect on zoxazolamine paralysis time, rat: 1092
 transformation, structure-activity relationship, hamster embryo cells: 1553
 BERYLLIUM
 bone sarcomas, rabbit: 1133, 1134
 calcined beryllium oxides, toxicity (rodent) and lung tumors (rat): 2312
 ores, toxicity and lung tumors, animal: 678
 BETEL CHEWING
 esophagus cancer, Ceylon: 2081
 mouth cancer: 2313
 Papua-New Guinea: 693, 2532
 upper g.i. cancer, Natal (Durban), ethnic groups: 1656
 BICYCLO(2.2.0)HEXA-2,5-DIENE, HEXAMETHYL-
 leukemia or liver tumors, mouse: 1478
 BILIARY TRACT
 dimethylaminoazobenzene metabolism, rat: 65
 BILIARY TRACT DISEASES
 cholelithiasis, gallbladder cancer, Finland: 899
 BILIARY TRACT NEOPLASMS
 epidemiology
 Germany (Göttingen-Weende): 1360
 sex ratio, England/Wales and western Europe: 1389
 induction, Thorotrast, human: 2170, 2172
 BIPHENYL
 poisoning, rat: 2232
 BIPHENYL, p-AMINO-
 occupational exposure, bladder cancer: 929
 BIPHENYL, 3:2'-DIMETHYL-4-AMINO-
 mammary tumors, LDH isozymes, rat: 55
 BIPHENYL, N-HYDROXY-4-ACETYLAMINO-, SULFURIC ACID ESTER
 mutagenesis, bacteria: 2239
 4-BIPHENYLACETAMIDE, 4'-FLUORO-
 kidney tumors, growth rate, rat: 1858
 N-4-BIPHENYLYLACETAMIDE, N-ACETOXY-
 synthesis: 2238
 BITTNER VIRUS (See under Virus, mammary tumor)
 BLADDER
 cell growth rate, effect of ethylsulfonyl-naphthalene-1-sulfonamide, mouse: 1167
 effect of
 diphenylhydantoin, rat: 1912
 sucrose, saccharin or cyclamate, mouse: 2315
 BLADDER CARCINOGENESIS
 aminobiphenyl, occupational: 929
 aminodibenzofuran, mouse: 2253
 animal, review: 993
 aromatic amines
 environmental and occupational: 1119
 mechanism, review: 1440
 bracken fern extracts, mouse or rat: 68, 1781, 2314
 cyclamates
 mouse: 407

BLADDER CARCINOGENESIS (contd.)

- possible, U.S.: 2544
- rat, review: 573
- detergent additives (acenaphthenes), mouse: 1772
- dibutyl nitrosamine
 - hamster: 1537
 - rat: 244
- 4-diphenylamine, rabbit: 1850
- ethylsulfonylnaphthalene-1-sulfonamide
 - mouse: 724, 993, 2253
 - rat: 2254
- fluorenylacetamide
 - mouse: 2253
 - rabbit: 1850
 - rat: 1171
- historical review: 562
- hydroxyanthranilic acid
 - carcinogen distribution, rat: 1474
 - effect of ascorbic acid, mouse: 423, 1473, 1931
 - related compound, effect of ascorbic acid, mouse: 1473
- hydroxyfluorenylacetamide, age factors, rat: 2249
- β -naphthylamine
 - dog: 4, 722, 2236
 - human: 4, 545
 - rabbit: 1850
- N-(4-[5-nitro-2-furyl]-2-thiazolyl)formamide
 - mouse: 1908
 - rat: 427, 1556
- 4-nitrosamino-4-n-butyl-n-butanol
 - rat: 1156, 1536
- non-industrial chemicals, review: 570
- occupational, human: 544, 545, 570, 924, 929, 1119, 1782
- phenacetin abuse, human: 1123, 2545
- saccharin, mouse: 1780
- tobacco, review: 1714, 1715
- tryptophan metabolites
 - effect of ascorbic acid, mouse: 239, 423, 1473, 1931
 - review: 5

BLADDER NEOPLASMS

- cinnabaric acid excretion, human: 1196
- epidemiology
 - artificial sweeteners including cyclamates, U.S.: 2544
 - benzidine or β -naphthylamine exposure, U.S.: 545
 - occupational, Britain: 544
 - U.S.: 545
 - phenacetin abuse, Sweden: 1123, 2545
 - review: 532
 - smoking, U.S.: 1337, 2544
- excretion of carcinogenic tryptophan metabolites, human: 70, 1195, 1196
- malignant or preinvasive, karyotype: 342
- occupation, smoking and tryptophan metabolites, tumor pathology: 690
- papilloma, risk of malignant transformation, review: 1449
- ploidy and DNA content, invasive or non-invasive tumors: 922
- recurrence rate, tryptophan metabolism, human: 1162

BLADDER NEOPLASMS (contd.)

- rubber exposure, Britain: 544
 - transitional cell carcinoma, exfoliative cytological diagnosis, stand: ds: 2660
 - urinary chemiluminescence, smokers: 1100
- BLOOD CELLS
- cell lines, cloning efficiency, chromosomes and herpes-type virus, normal subjects or pts. with non-malignant diseases: 2631
 - peripheral WBC cultures, chromosomes, normal human: 1710
 - RBC, nature of membrane polyoma virus receptors, human: 2466

BLOOD COAGULATION

- effect of aflatoxin, rat: 1107

BLOOD DISEASES

- infectious mononucleosis
 - Epstein-Barr virus, review: 1443
 - induction, Epstein-Barr virus (from Burkitt lymphoma cultures), human cancer: 1643
 - peripheral WBC cell line, transplantable hamster tumor (H-RKB2): 1709
 - serum Epstein-Barr virus antibodies: 1613

BLOOD GROUPS

- A, B and H antigens
 - mixed-cell agglutination reaction, lung cancer: 2626

ABO

- female genital cancer, Poland: 550, 551
- larynx cancer, East Germany: 1670
- lung cancer, smoking, Wales: 904
- stomach cancer, Poland (Cracow): 2550

Gc

- leukemia: 2595
- Poland: 1397

Gm

- female genital cancer, Poland: 550, 551
- haptoglobin genotype
- leukemia: 2595

Rh

- female genital cancer, Poland: 550, 551
- larynx cancer, East Germany: 1670
- lung cancer, smoking, Wales: 904

Xg type

- Ph⁺-positive or -negative chronic myeloid leukemia: 1394, 1398

BLOOD PRESSURE

- effect of deoxycorticosterone, methylcholanthrene-induced tumors, rat: 2194
- Goldblatt-type hypertension, effect of methylcholanthrene, rat: 2193

BLOOD PROTEINS

- effect of o-aminoazotoluene, mouse: 2234
- lipoproteins and α_1 -globulin, rat with transplanted hepatoma: 1708
- neoantigen, aflatoxin-induced, rat: 2293
- serum α -fetoprotein, liver or testicular tumors, human, review: 2134

BONE

- gallium distribution, leukemic or nonleukemic AKR/J mice: 1775
- leukemia virus particles, high-leukemia mouse strains (AKR and C3H/Fg): 1981
- osteomyelitis with fistula, skin cancer at fistula scar: 2158
- ⁹⁰Sr levels, USSR (all ages): 1453

BONE DISEASES

fibrous dysplasia, malignant transformation:
339

BONE MARROW

cells
effect of MC29 avian leukosis virus, chicken:
779
site of Friend virus susceptibility locus,
mouse: 1217

chromosomes

atomic radiation exposure (Hiroshima),
healthy or leukemic persons: 591, 592
radiation effects, rat: 590
toxicity, methyl nitrosourea, mouse: 1557
transplantation, effect on dimethylbenzanthracene
lymphoma, mouse: 377

BONE MARROW DISEASES

erythroid hyperplasia or myelofibrosis,
leukemia virus particles, cat: 761
myelofibrosis with myeloid metaplasia, saponin
induction, rabbit: 1163
Rauscher leukemia virus-induced, rat: 772

BONE NEOPLASMS

arrhenoblastoma, familial: 947
atomic radiation exposure, Hiroshima/Nagasaki:
1027

chondrosarcoma

joints, Maffucci's syndrome: 965
possible viral etiology, human: 815

epidemiology

children, U.S., ethnic groups: 1682
dogs, USSR (Moscow): 2098
East Germany: 2090

induction

benzpyrene, rat: 2198, 2200
methylcholanthrene, rat: 2198
nitroquinoline oxide, rat: 2198
rabbit: 1028
⁹⁰Sr, swine: 26

osteogenic sarcoma

beryllium induction, rabbit: 1133, 1134
familial: 1331
radiation-induced, child: 588

osteoma

skull, induction, hormones and/or gold
thioglyucose, mouse: 718

osteosarcoma

age factors, skeletal growth rate: 2089
dimethylbenzanthracene-induced, hormone
effects, rabbit: 2231
Moloney- or Harvey sarcoma virus-induced,
rat or hamster: 811, 2364
possible viral etiology, human: 815
Rous sarcoma virus-induced, marmoset: 798

radiation-induced

maxillary carcinoma, familial basal cell
nevus syndrome: 2163
occupational or therapeutic exposure, human:
1452

sarcoma

malignant transformation of fibrous dysplasia:
339
mother and son, familial polyposis of colon:
2655
serum sarcoma-specific antigens, pts. and
their relatives: 1591

BONE NEOPLASMS (contd.)

site of injury, Paget's disease: 1404
BRACKEN FERN (See Pteris aquilina)

BRAIN

acute cerebellar encephalopathy, association
with neuroblastoma, cases and review: 2104
astrocytes or choroid plexus cells, polyoma
virus transformation, hamster: 2460
effect of
leukemia viruses, age factors, mouse: 2331
methyl nitrosourea, fetal rat: 1876, 1879
immunity disorder, induction, syngeneic
transplantable leukemia, mouse: 2331
injury by carcinogen implantation, obesity,
mouse: 620
progressive multifocal leukoencephalopathy,
polyoma virus-like particles, chronic
leukemia, case: 2471
short-wave irradiation and other CNS-acting
treatment, effect on methylcholanthrene
tumors, rat: 2192
toxicity, cycasin, mouse: 2303
BRAIN NEOPLASMS (See also Nervous system neoplasms)
epidemiology
children, Hungary: 1348
geographical variations, Denmark and U.S.:
1684
Minnesota: 2579, 2580
Poland (Cracow), temporal fluctuations:
2582
review: 992
South Africa (Transvaal), ethnic groups:
2581
induction
animal, review: 17, 992, 1736
benzpyrene, rat: 234, 1094
dimethylbenzanthracene, rat: 1819
ethyl nitrosourea, transplacental, rat:
635, 637, 2283
fluorenylacetamide, rat: 1849
lipids, mouse: 1493
methylcholanthrene
mouse: 1048, 1051, 2189
virus-like particles: 822, 1297,
1567, 1621
rat: 234
methyl nitrosourea
dog: 1153
rabbit: 242, 253, 254, 1519, 1877, 1878
rat: 37, 631, 632, 633, 1876, 1877,
1880, 1881, 2269, 2270, 2283, 2284
transplacental: 634
nitroso compounds, transplacental, rat:
1191
phenyldimethyl triazene, rat: 2269, 2270
Rous sarcoma virus, dog: 797, 1240
simian adenovirus (SA7), hamster: 305,
482, 2414
trimethylbenzanthracene, rat: 632
injury, child: 1738
meningeal fibroma and brain tumors, induction,
bovine papilloma virus, calf: 1268
stimulation, radiotherapy or antitumor agent,
human: 1747
tumor cell lipids, structure and antigenic
activity: 1429

- BREAST NEOPLASMS (See Mammary neoplasms, human)
- BROMODEOXYURIDINE (See under Antitumor agents)
- BRONCHUS
- effect of cigarette or cigar smoke: 737
- BRONCHUS NEOPLASMS
- cell growth kinetics, measurement method: 2614
 - epidemiology
 - air pollution, East Germany: 2543
 - Poland (Gliwice), women: 535
 - smoking, East Germany: 526, 2543
 - urbanization, East Germany: 527
 - methylmitrosourea-induced, rat: 37
 - scleroderma: 2153
 - serum adenovirus-18 antibodies: 834
- BURNS (See under Injuries or Scar tissue)
- BUSULFAN (See under Antitumor agents)
- BUTANE, DIEPOXY-
- effect on DNase-II, cell-free system: 612
- n*-BUTANOL, 4-NITROSAMINO-4-*n*-BUTYL-
- bladder tumors, rat: 1156, 1536
- BUTTER YELLOW
- Hodgkin's-like lymphoma, rat: 732
- β -BUTYROLACTONE
- effect on DNase-II, cell-free system: 612
- CADMIUM
- analysis, cigarette tobacco and smoke: 686
 - s.c. sarcoma, enzymes, rat: 235
 - serum and tissues, lung and other cancer, human: 1135
- CALCITONIN
- adrenal medulla, possible significance in multiple endocrine tumor syndrome (Type 2): 2651
- Cannabis CONSTITUENTS
- analysis
 - cigarette smoke: 1765
 - mouth and fingers of marihuana smokers: 1766
 - effect on human WBC cultures: 2316
- CANTHARIDIN
- skin tumor promotion, mechanism, mouse: 1817
- CARBAMATES (See also Urethan)
- butyl or isoamyl carbamate, effect on urethan lung tumors, mouse: 1082
 - lung tumors, bioassay method, mouse: 410
 - zinc-dithiocarbamic acid type herbicides, lung tumors, mouse: 1778
- CARBAMIC ACID, 1,1-DIPHENYL-2-PROPYNYL-N-CYCLOHEXYL-
- multiple tumor types, rat, mouse or gerbil: 1563
- CARBOHYDRATES
- intolerance, endometrial cancer: 1357, 1431
 - transport, Harvey sarcoma virus-infected (hamster, human or mouse) or -transformed (rat) cells: 2360
 - uptake, mouse sarcoma virus-transformed mouse embryo cells: 463
- CARBON TETRACHLORIDE
- effect on liver regeneration, mouse: 1491
 - hepatoma, rat, strain difference: 420
 - toxicity, liver, mechanism, rat: 1860
- CARCINOGENESIS (general and unspecified)
- gene-selection theory, review: 559
- CARCINOGENESIS (general and unspecified) (contd.)
- 2-hit and multiple-hit theories, mathematical models: 896
 - mechanism, theory, review: 12
 - RNA viruses, mechanism, review: 8
- CARCINOGENESIS, CHEMICAL
- abnormal responses of non-hemocytic cells of midgut and hindgut, benzpyrene-induced, cockroach: 625
 - acylarylhydroxylamines, structure-activity relationship, rat: 2251
 - aliphatic azo compounds and triazenes, structure-activity relationship, rat: 1193
 - aromatic compounds, structure-activity relationships, review: 353, 997
 - azobenzene derivatives, structure-activity relationships, review: 571
 - brain, animal, review: 17, 1736
 - caustic chemicals + radiotherapy, lupus vulgaris malignant transformation: 595
 - cell growth kinetics, animal, review: 2127
 - comparison with viral carcinogenesis, review: 577
 - DNA and RNA methylation, review: 567
 - epoxides, lactones and halo-ethers, mechanism, animal, review: 1001
 - hamster cheek pouch, cell growth kinetics, review: 2125
 - hormones, role of pituitary-adrenal system, review: 2120
 - hydrocarbons, mechanism, review: 2123
 - inhibition, mechanism, review: 1008
 - juvenile hormone-like substances, melanotic tumors, *Drosophila*: 1194
 - mechanism, review: 352, 1439, 2122, 2155
 - metals, human, review: 996
 - mouse cervix, epithelial-mesenchymal interactions: 2113
 - neoblastic tumors, planaria: 627
 - 4-nitroquinoline-1-oxide and related agents, structure-activity relationship: 1477
 - nitroso compounds, transplacental, rodent, review: 1005
 - occupational, review: 6
 - polyvinylpyridine N-oxide, mouse or rat: 717
 - review: 1019, 1021
 - skin, mouse, review: 2124
 - steroid hormones, endocrine tumors, review: 999
 - tumor-specific transplantation antigens, review: 1442
 - urethan, dimethylbenzanthracene or methyl-cholanthrene, hamster strain (*Phodopus sungorus*): 2642
 - effect of influenza virus, mouse: 1619
- CARCINOGENS, CHEMICAL
- analysis, margarine or chocolate, processing methods, Germany: 604
 - antagonists and inhibitors, mechanism of action, review: 1008
 - bacterial or fungal, occurrence, review: 162, 163
 - bronchial epithelial cell abnormalities, classification: 2319
 - chromosomal abnormalities, classification, review: 1002

CARCINOGENS, CHEMICAL (contd.)

- chronic toxicity tests, animal, methods: 1759
- detection of weakly active carcinogens, method: 1190, 1771
- dietary, g.i. and liver tumors, review: 1014
- DNA alkylation, mechanism, review: 1011
- dose-response relationship, mathematical model, animal lung tumors: 1559
- effect on
 - cell growth kinetics, malignant transformation, review: 1450
 - skin, intramitochondrial dense body, mouse: 2184
- environmental
 - liver cancer, international: 2561
 - lung or esophagus cancer, South Africa, ethnic groups: 928
 - nasopharynx cancer, review: 568
 - permissible limits: 736
- evaluation methods, mathematical model, review: 2130
- foods, analysis, review: 161
- free radical formation, organic solvents or water: 598
- mutagenesis
 - Drosophila*: 1760
 - screening method, mouse: 1555
- non-industrial chemicals, bladder cancer, review: 570
- occupational exposure
 - cancer epidemiology
 - anesthesiologists, U.S. and Canada: 888
 - chemists, U.S.: 933
- screening
 - cell cultures, review: 1007
 - dog and rodent, review: 7
 - results, review (book): 1022, 1023
- skin tumors, screening method, mouse: 1463
- teratogenesis, animal, review: 2129
- thymic lymphoma, possible leukemia virus, mouse: 1203
- transformed hamster embryo cells, LDH isoenzyme patterns: 1561

CAROTID BODY NEOPLASMS

- chemodectoma, familial bilateral, case and review: 2653

CELL GROWTH KINETICS

- adenovirus 7- or SV40-adenovirus 7-transformed cells: 2470
- aflatoxin- or fluorenylacetamide-induced pre-malignant liver nodules, rat: 671
- ascites or solid mouse tumors: 138, 1693
- benign or malignant thyroid tumors, animal: 2119, 2629
- breast cancer: 538, 2100, 2612
- bronchogenic carcinoma, review: 1451
- carcinogen-induced skin tumors, mouse: 537, 1057, 1514, 1515
- cervix cancer: 136, 986, 1695, 2570, 2611
- cell lines: 141, 142
- chemical carcinogenesis, animal, review: 2125, 2127
- cloning efficiency
 - mouse lymphoma or plasmacytoma cells: 2640
 - WBC cell lines from normal subjects or cancer pts.: 2631

CELL GROWTH KINETICS (contd.)

- diethylnitrosamine hepatoma, guinea pig: 654
- dimethylbenzanthracene mammary tumors, rat: 708, 709, 1824, 1825, 2228
- DNA contents
 - mosaicism, premalignant or malignant skin tumors: 923
 - non-invasive or invasive bladder cancer: 922
- effect of
 - basic polymers and dyes, transformed cells: 147
 - enzymes, transformed cells: 148
 - estrus cycle, mouse tumor: 137
 - ethylsulfonylnaphthalene-1-sulfonamide, bladder, mouse: 1167
- fluorobiphenylacetamide kidney tumors, rat: 1858
- glucose and lactate metabolism, high- and low-tumor-producing mouse cell clones: 345, 347
- glutathione biosynthesis and carcinogenesis, review: 2122
- goitrogen-stimulated thyroid, rat: 333
- growing and regressing Moloney viral sarcoma, mouse: 1590
- growth enhancement, substance from leukemic or normal cells, mouse embryo cells: 975
- hepatoma-susceptibility genotype effects on liver, mouse: 2618, 2619, 2620
- Hodgkin's disease: 536
- host immunity, animal or human tumors: 945
- human cancer
 - lung and lymph node metastases: 539
 - mathematical model: 946, 2100, 2613, 2614, 2615
 - method of studying DNA synthesis: 1420
- human leukemia: 540, 921, 982, 2099
- induced tumors and corresponding normal tissue, mouse or rat: 920
- kidney, effect of mammary tumor virus in vitro, mouse: 2394
- Krebs cycle metabolites, growth stimulation, tumor cells in vitro: 615
- liver regeneration, normal or mammary tumor-bearing mouse: 941
- lung, urethan susceptibility, mouse or hamster: 2287
- malignant transformation in vitro and in vivo, review: 1450
- mammary gland, effect of estrus cycle, rat: 2616
- tumors, effect of epithelial growth factor in vitro: 139
- mathematical models
 - asbestos-induced mesothelioma, rat: 1340
 - human cancer: 946, 2100, 2613, 2614, 2615
 - irradiated exptl. tumor in vivo: 940
 - mouse sarcomas: 2050
 - tumor cell populations: 942
- medium pollution, cell cultures: 980
- mouse hepatomas: 2617
- normal, transformed and malignant cells, review: 587, 1006
- polyoma virus-transformed or tumor cells: 865, 866, 2470

CELL GROWTH KINETICS (contd.)

- preinvasive or malignant tumors, karyotype: 342
- protein synthesis, mouse tumor: 1701
- psychokinetic study, exptl. mammary tumor: 985
- radiation carcinogenesis, animal, review: 2125, 2126, 2127
- rat hepatoma: 140, 1341, 1534, 1694
- Rauscher viral leukemia, mouse: 775
- regenerating limb, effect of liver ribonucleoprotein, frog: 984
- sarcoma virus-infected or -transformed cells: 791, 1961, 2366, 2386
- Sendai virus-infected cells: 317
- Shope papilloma virus-induced tumors, rabbit: 2473
- skin tumors or premalignant lesions, human: 1339
- spontaneous malignant transformation, rat fibroblast cultures: 2101
- stomach cancer, role of intestinal metaplasia or ulceration: 939
- SV40-transformed cells: 2436, 2470
- syngeneic or allogeneic host-mammary tumor systems, mouse: 2627
- thymus, radiation leukemia, mouse: 2164
- tissue growth-stimulating or -retarding substances, normal or malignant cells, review: 563, 564
- tobacco smoke-exposed mouse lung or kidney cells: 1211
- transplanted tumor or regenerating liver, effect of urethan, mouse: 621
- tumors induced by prenatal irradiation, latent periods, children: 2169
- viral carcinogenesis, animal, review: 2126
- CERESIN (See under Wax, medicinal)
- CERIUM HYDROXIDE
 - dust, lung cancer, radon exposure, rat: 2171
- CERVIX UTERI
 - contraceptive hormone effects on nucleic acid and protein synthesis, human: 1425
- CERVIX UTERI NEOPLASMS
 - carcinoma in situ, growth rate: 342, 1695
 - cell lines, karyotype and growth kinetics: 141, 142, 2632
 - chromosomes: 342, 1396
 - early invasive form, chromosomes, review: 1722
 - epidemiology
 - Canada: 894, 2569, 2570
 - contraceptives, Czechoslovakia: 911
 - early lesions, methods: 519
 - Germany (Munich) and Japan (Osaka), hormonal status: 1690
 - herpesvirus type 2 infection, Texas (Houston) or Georgia (Atlanta): 510, 2576
 - India: 1363, 2573
 - intrauterine contraceptive devices, Japan: 1455
 - Kentucky (Louisville): 135, 2571
 - microinvasive carcinoma, Ohio (Cleveland): 1361
 - Natal, ethnic groups: 1689
 - New York City, hormonal or mechanical contraceptives: 1387

CERVIX UTERI NEOPLASMS (contd.)

- New Zealand, ethnic groups: 2572
- Poland: 520, 910, 2624
- reproductive histories, U.S.: 906, 907, 2568
- review: 356, 1721
- South Africa (Cape Town), ethnic groups: 908
- tubal-ligation sterilization, Puerto Rico: 2574
- USSR (Krivoi Rog), methods: 2575
- Utah: 1352
- growth kinetics: 136, 141, 142, 342, 986, 1695, 2570, 2611
- herpesvirus Type 2 (genital) antibodies: 510, 2043, 2576
- induction
 - dimethylbenzanthracene alone or + contraceptives, mouse: 1128
 - epithelial-mesenchymal interactions, mouse: 2113
 - estradiol, rat: 707
 - hormonal contraceptive, mouse: 715, 1554
 - methylcholanthrene, rat: 707
 - plastics, mouse: 1836
 - possible, estrogen-progestagen contraceptive, human: 1127
 - radiation and/or benzpyrene, mouse: 1036
- injuries, human: 1737
- pathogenesis: 987
- possible induction by spermatic DNA: 706
- postoperative vaginal reconstruction, malignant transformation, case: 2658
- premalignant dysplasia
 - azathioprine-induced, human: 705
 - contraceptive hormone effects on DNA, RNA and protein: 1425
- radiotherapy-induced reticulum cell sarcoma: 1745
- risk of second primary tumor, Connecticut: 909
- serum adenovirus-18 antibodies: 834
- viral etiology, review: 576
- CHEEK POUCH NEOPLASMS
 - induction
 - avian adenovirus (CEL0)-transformed human amnion cells, hamster: 833
 - dimethylbenzanthracene, hamster: 373, 694, 695, 696, 697, 1075, 1076, 1802, 1813, 1926, 2225, 2229, 2230
 - lymphoma-like, induction, vitamin A palmitate, hamster: 1164
 - SV40-induced, pathology, hamster: 1281, 1282
- CHLORAMPHENICOL
 - effect on
 - diethylnitrosamine liver tumors, rat: 1869
 - methyl dimethylaminoazobenzene liver tumors, rat: 1893
 - leukemia, human: 733, 734
- CHLOROQUINE
 - effect on skin carcinogenesis, mouse: 1486
- CHLORTETRACYCLINE
 - skin tumor promotion, mouse: 2195
- CHOLANTHRENE
 - transplanted sarcoma, effect of immune serum, mouse: 623

4-CHOLESTEN-3-ONE, 6 β -HYDROXY-

s.c. tumors, mouse: 1936

CHOLESTEROL

brain tumors, mouse: 1493

effect on

methylcholanthrene tumors, mouse: 1064

protein synthesis, human WBC: 1192

CHOLESTEROL PALMITATE POLYMER

s.c. sarcoma, mechanism, rat: 1544

CHOLIC ACID

hamster tumor, viability in vitro at high

temperature: 500

CHROMOSOMES

abnormalities

cancer pts. and normal population: 956

cervix cancer: 1396

Ch¹ anomaly, chronic lymphocytic leukemia,

familial: 934

dimethylbenzanthracene-induced leukemia or

preleukemic changes, rat: 729

human cancer, review: 1003, 1010

Klinefelter's syndrome, breast cancer: 1400

leukemia risk, review: 585

malignant lymphoma and myeloma, review:
2151

mongolism

lymphocyte transformation rate: 1402

with leukemia, possible leukemia virus,
review: 1026

child: 953, 1406

occupational benzene exposure, age factors:
952

tobacco smoke-exposed mouse lung or kidney
cells: 1211

acute leukemia, review: 2152

autonomy and malignancy of induced thyroid
tumors, rat: 2629

benzene-induced leukemia, human: 951, 1120

breakage, induction, radiation or radiomimetic
compounds, plant: 1399

carcinogen binding, rat liver: 1066

cervix cancer, review: 1722

chronic leukemia: 2635, 2636

congenital anomalies, leukemia, human, review:
1733

diethylnitrosamine hepatoma, guinea pig: 654

dimethylbenzanthracene leukemia, rat: 374

DNA content, normal or leukemic human WBC:
982

virus-induced tumors, review: 1732

EB virus-infected human cells: 297

effect of

Cannabis alkaloids, human WBC cultures:
2316

carcinogens, review: 1002, 1716

cyclamates, human WBC: 403

luteoskyrin, tumor cells: 1172

nitrogen mustard derivative, Rous sarcoma
virus-transformed rat cells: 796

nitroquinoline oxide, rat tumor cells:
1864

viruses, mechanism, review: 1002

genotypic mosaicism, mammary tumors, allophenic
mice: 159

griseofulvin-induced leukemia, human: 1201

Gross leukemia virus-transformed rat thymus
cells: 2065

CHROMOSOMES (contd.)

group 17/18, RES tumors, review: 1015

Harvey virus-transformed mouse or rat cells:
280

HeLa cell lines: 2630

hetero- and homotransplanted hamster or human
tumors: 2664

human cervix carcinoma cell line: 2632

leukemia and lymphoma cell lines: 320,
978, 2114, 2638

L2C guinea pig leukemia: 2633

lung tumors or smoking-induced respiratory
epithelial hyperplasia: 684

malignancy-associated changes, peripheral
neutrophils, lung cancer: 949

markers

Burkitt lymphoma: 158, 341

transformed human cell lines, herpes-type
virus: 88

methylcholanthrene-induced tumors

hamster: 221

rat: 1053

skin, mouse: 1054

methylnitrosourea- or trimethylbenzanthracene-
induced brain tumors, rat: 632

mineral oil + androgen-induced leukemia, mouse:
406

mosaicism, premalignant or malignant skin
tumors: 923

mouse lymphoma or plasmacytoma cell lines:
2640

nitroquinoline oxide-transformed hamster cells:
1863

non-invasive or invasive bladder cancer: 922

peripheral WBC cell lines, human: 2631, 2662,
2663

Ph¹, chronic granulocytic leukemia: 156, 157,
1394, 1398

³²P-induced mouse leukemia: 1454

plastic implant tumors, mouse: 2300

ploidy

endometrial carcinoma: 1395

growth kinetics, cervix cancer, human: 2611

melanoma: 1393

methyltrimethylaminoazobenzene rat hepatoma
nuclei: 1141

tumor growth rate, methylcholanthrene s.c.
sarcoma, mouse: 1514

WBC, occupational radiation exposure: 1030

polyoma virus-infected mouse cells: 493

radiation effects

healthy persons exposed to atomic bomb,
Hiroshima: 591

rat bone marrow: 590

radiation-induced leukemia

human: 592, 1031, 1405, 1460, 1757, 2165

mouse: 361, 1033

rat embryo cells transformed by diethyl-
nitrosamine + Rauscher leukemia virus: 776

Rous sarcoma virus-induced hamster or mouse
tumors: 112, 453, 799

Sendai virus-infected hamster embryo cells:
317

sarcoma-inducing, spontaneously transformed
rat embryo cell cultures: 2628

sex

genital, breast and other tumors, women: 955

CHROMOSOMES (contd.)

- mosaicism, acute myeloid leukemia: 954
- lung cancer, SV40 transformation of WBC and fibroblast cultures: 2456
- relation to trophoblastic proliferation, hydatidiform mole: 331
- testicular teratomas from male or female embryo tissue grafts, mouse: 957
- uterine carcinoma: 2661
- spontaneous or benzpyrene-induced tumors, rat: 1053
- SV40-transformed human cells: 1607, 2455
- transforming mouse embryo cells, effect of culture medium: 346
- transplantable sarcoma, strain differences, rat: 2665
- treated or untreated polycythemia vera: 2641
- trisomy-G, acute erythroleukemia: 2637
- tumors from transformed cells, mouse: 160
- urethan lymphoma, mouse: 77, 238
- viral or spontaneous leukemia, mouse: 361, 1734, 1735

CHRYSENE

- metabolism, effect of methylcholanthrene, rat liver microsomes: 1049

CIGARETTE SMOKING (See Tobacco smoking)

CINNAMALDEHYDE, 3,5-DIMETHOXY-4-HYDROXY-nasopharynx cancer, review: 1004

CITRAL (See 2,6-Octadienal, 3,7-dimethyl-)

CLAUDE'S CHICKEN TUMOR VIRUS 10 (See under Virus, sarcoma)

CLUSTERING (See under Disease outbreaks)

COAL DUST

- air pollution
- lung cancer, England and Wales: 1660
- stomach cancer, England and Wales: 1661
- occupational exposure, lung cancer, smoking, Scotland: 1659

COCARCINOGEN A-1

- epidermal hyperplasia, mouse skin: 1188

COCARCINOGENESIS

- alkylbenzenesulfonates, stomach, rat: 1476
- mechanism, review: 1020
- tobacco smoke, skin, mouse: 35

COCARCINOGENS, CHEMICAL

- cell culture test: 1761
- effect on threshold response to skin carcinogens, mouse: 1087
- phenols, excretion, germ-free or conventional rats: 1489
- unburned tobacco, skin tumor promoters, mouse: 1542

COLCHICINE

- mutagenesis and effect on tumor incidence, *Drosophila*: 626

COLLAGEN

- content, spontaneously transformed mouse or rat embryo cells: 981

COLON

- familial polyposis
- associated bone sarcomas, mother and son: 2655
- Gardner's and Turcot's syndrome: 2654
- soft tissue sarcomas, multiple-case family: 958
- malignant transformation: 336, 958, 964, 1332, 2103

COLON (contd.)

- Peutz-Jeghers syndrome, sex cord tumor of ovary: 1403

COLON NEOPLASMS

- epidemiology
- appendectomy, West Germany: 2587
- California (Los Angeles), ethnic groups: 2556
- Denmark (Copenhagen): 898
- familial polyposis: 336, 958, 964, 1332, 2103, 2558, 2672
- Jamaica: 2557, 2622
- single- or multiple-"hit" model: 2085, 2086
- Tennessee (Nashville), ethnic groups: 2555
- nuclear RNA fractionation: 950
- polyps
- risk of malignant transformation, review: 1449
- smoking: 1485
- villous adenoma, frequency of second primary tumors: 963

CONNECTIVE TISSUE

- mesenchyme, development of transplanted mammary tumors, mouse: 2646
- ⁸⁵Sr or ⁹⁰Sr retention, dosimetry, dog: 1753
- toxicity, aflatoxin or sorbic acid, rat: 699

CONNECTIVE TISSUE DISEASES (See also Immunity disorders)

- Maffucci's syndrome, malignant transformation: 965

CONNECTIVE TISSUE NEOPLASMS

- epidemiology
- East Germany: 2090
- Kaposi's sarcoma, Nigeria: 1371
- Tanzania (mainland): 134
- rhabdomyosarcoma, children, Mexico City: 1362
- familial cancer syndrome, children, U.S.: 1334
- familial, multiple primary tumor syndrome: 914
- Gardner's syndrome type, associated familial colonic polyposis and Turcot's syndrome: 2654
- induction
- 5-acetamido-3-(5-nitro-2-furyl)-6H-1,2,4-oxadiazine, rat: 426
- methylcholanthrene, mouse: 974, 2191
- methylnitrosourea, dog: 1153
- mineral oil, transplantation, mouse: 1492
- nickel, rat: 704, 1177, 1178
- radiation, rabbit: 1028
- Rous sarcoma virus, marmoset: 798
- mesenchymal sarcomas of thyroid, epidemiology, Italy: 913
- mesothelioma, induction, MC29 (avian leukosis) virus-infected cells, chicken: 1994
- multicentric fibromatosis and desmoids, familial: 543
- sarcoma
- associated polyposis of colon, multiple-case family: 958
- interferon-antagonistic factors, human: 467
- serum sarcoma-specific antigens, pts. and their relatives: 1591
- virus-like particles, human: 468, 815, 1592

CONNECTIVE TISSUE NEOPLASMS (contd.)

- spindle cell sarcoma, runtng syndrome, mouse: 1200
 - spontaneous myxofibroma, C-type virus particles, snake (*Vipera russelli*): 471
 - uterine leiomyosarcoma, androgen + estrogen-induced, hamster: 1833
- CONTRACEPTIVES, HORMONAL
- breast cancer, human: 1125
 - cervix cancer: 1127
 - Czechoslovakia: 911
 - mouse: 715, 1554
 - New York City: 1387
 - effect on
 - chemical mammary carcinogenesis, rat: 56
 - mammary tumor incidence, mouse: 1503
 - nucleic acid and protein synthesis, human cervix: 1425
 - female genital cancer, review (book): 557
 - fibroadenoma of breast, human: 1126, 1806, 1831
 - mammary and genital tumors, animal and human, review: 2
 - multiple tumor types, rat: 1830
 - osteoma of skull, mouse: 718
 - progestational agents, effect on dimethylbenzanthracene induction of cervix cancer, mouse: 1128

CONTRACEPTIVES, MECHANICAL

- cervix cancer
 - Japan: 1455
 - New York City: 1387

COPPER

- cupric acetate
 - effect on dimethylaminoazobenzene liver tumors, rat: 1137
 - liver enzyme response to carcinogen, rat: 2260
- sulfate, effect on dimethylbenzanthracene tumors, mouse: 210

CORPUS UTERI NEOPLASMS

- choriocarcinoma and related diseases
 - epidemiology, Australia (Sydney): 1367
 - Iraq: 1366
 - feedback hormonal metabolism and host immunity: 967
 - histology, chromatin-positive or -negative hydatidiform mole: 331
- endometrial cancer
 - chromosomes: 1395
 - high-risk groups, metabolic status: 1136, 1357, 1431
 - persistent ovarian stromal theca cells, postmenopausal women: 548
 - prognosis and histology: 2621
- epidemiology
 - Germany (Giessen), diabetes and hormonal factors: 1688
 - Japan (Osaka) and Germany (Munich), hormonal factors: 1690
 - Kentucky (Louisville): 2571
 - Ohio (Lucas County), review: 2071
 - Poland: 520
- growth kinetics, mathematical model: 2613
- induction
 - alkylnitrosoureas, pregnant rat: 713
 - methylcholanthrene, hormone effects, mouse: 1901

CORPUS UTERI NEOPLASMS (contd.)

- oral contraceptive, rat: 1830
 - plastics, mouse: 1836
 - leiomyosarcoma, induction, androgen + estrogen, hamster: 1833
 - possibly radiation-induced, human: 1037
 - radiation-induced ichthyosis uteri: 171
 - risk of second primary tumor, Connecticut: 909
 - sarcoma, induction, hydroxyaminoquinoline oxide, rat: 428
 - second primary tumor, risk, breast cancer, Connecticut: 909
 - serum adenovirus-18 antibodies: 834
 - sex chromosomes: 2661
- CORTICOSTEROIDS (See also specific compounds)
- effect on mouse mammary tumor virus: 116
- CORTICOSTERONE
- effect on aflatoxin metabolism, rat liver microsomes: 1115
- CORTICOSTERONE, DEOXY-
- effect on blood pressure and growth of methylcholanthrene tumor, rat: 2194
 - mammary nodule induction, effect of thymectomy, mammary tumor virus-infected mouse: 820, 821
- CORTISONE
- effect on urethan lung tumors, mouse: 1081
- CORTISONE ACETATE
- enhancement of dimethylbenzanthracene leukemogenesis, mouse: 1810
- COUMARIN COMPOUNDS
- detergent additives, skin tumors, radiation effects, mouse: 2301
 - effect on lung metastases, syngeneic mouse tumors: 1469
- Crotalaria spectabilis*
- pyrrolizidine alkaloid, liver toxicity, rat: 2308
- CROTON OIL
- epidermal hyperplasia, mouse skin: 1188
 - promotion of transplacental dimethylbenzanthracene skin tumors, mouse: 2329
 - skin tumor promotion, mechanism, mouse: 1817
 - toxicity, lung, mouse: 701
- CROTON OIL FACTOR A-1
- effect on DNA, RNA and protein, mouse skin: 1564
- CROTON OIL PHORBOL ESTERS
- cell culture test: 1761
 - effect on radiation-induced skin damage, mouse: 2299
 - phorbol myristate acetate, effect on RNA, mouse fibroblast line: 1471
 - skin tumor promotion, mechanism, mouse: 47, 208, 1784
- CYANURIC ACID (See s-Triazine-2,4,6-triol)
- CYCAD SEEDS
- toxicity, chick: 240
- CYCASIN
- carcinogenic and toxic effects, animal or human, review: 1017
 - kidney tumors
 - rat: 1774
 - tissue culture characteristics, rat: 258
 - Wilms' type, rat: 719

- CYCASIN (contd.)
 liver tumors and reticulum cell sarcoma,
 mouse: 2303
 toxicity
 brain, mouse: 2303
 conventional or germ-free rat, review: 995
- CYCASIN AGLYCONES (methylazoxymethanol)
 carcinogenic and toxic effects, animal or
 human, review: 1017
 effect on serum proteins, monkey: 62
 toxicity, mouse or rat: 1924
- CYCLAMATES
 bladder tumors
 mouse: 407
 rat, review: 573
 U.S.: 2544
 effect on
 chromosomes, human WBC: 403
 g.i. tract, mouse: 2315
- CYCLOHEXANE, HEXACHLORO-
 transplacental, effect on embryonic kidney or
 lung, mouse, review: 2128
- CYCLOHEXYLAMINE
 and derivatives, effect on chromosomes, human
 WBC: 403
- CYCLOPHOSPHAMIDE (See under Antitumor agents)
- CYCLOPROPENE COMPOUNDS (See also Fatty acids,
 cyclopropenoid)
 combined with aflatoxin, hepatotoxicity, trout:
 665
- CYTOSINE ARABINOSIDE (See under Antitumor agents)
- DDT
 toxicity, lung, mouse: 701
- DETERGENT ADDITIVES
 acenaphthenes, metabolism (dog) or carcinogenic
 effects (mouse and rat): 1772
 "brighteners," skin tumors, radiation effects,
 mouse: 2301
- DEXAMETHASONE
 effect on Rous virus sarcoma induction, baboon:
 457
- DIABETES MELLITUS
 cancer epidemiology
 Germany (Stralsund): 891
 Massachusetts: 2519
 endometrial cancer: 1357, 1431
 female genital cancer, Germany (Giessen): 1688
 oropharynx cancer, U.S.: 1384
 pancreas cancer, Scotland (northeastern): 1666
- DIENESTROL
 effect on dimethylbenzanthracene osteosarcoma,
 rabbit: 2231
- DIESEL EXHAUST PRODUCTS (See under Engine exhaust
 gases or Petroleum and petroleum products)
- DIET (See also under Foods)
 high-fat and/or low-protein, hepatoma, mouse
 or rat: 250, 673
 iodine-deficient, with ¹³¹I, thyroid tumors,
 effect of hypophysectomy, rat: 2265
 lipotrope-deficient, effect on aflatoxin
 hepatocarcinogenesis, rat: 188
 pyridoxine-deficient, serum α_1 -fetoprotein,
 primate: 970
- DIETARY FACTORS (See also under Foods)
 effect on radiation tumor incidence, mouse:
 1461
 esophagus cancer
 Jamaica and Australia, comparison: 2533
 Puerto Rico: 932
 South Africa (Transkei), ethnic groups:
 1121, 1122
 leukemia, Europe, review: 2135
 liver cancer, Africa: 970, 2084
 oropharynx cancer, Puerto Rico: 932
 protein intake, stomach or intestinal cancer,
 international: 1432
 pyridoxine deficiency, liver cancer epidemiology
 Africa: 970
 stomach cancer epidemiology, Iceland: 2083
 thyroid cancer, world, review: 2133
 urinary tryptophan metabolites, Africa (Uganda):
 1368
- DIETHYLSTILBESTROL
 effect on
 aflatoxin liver carcinogenesis, rat: 1110
 dimethylaminoazobenzene tumors, rat: 2264
 dimethylbenzanthracene tumors, rat or
 hamster: 696, 1822, 2264
 kidney tumors, enzymes, hamster: 72
 leiomyosarcoma of ductus deferens, hormone-
 independent variants, hamster: 1130
 mammary carcinogenesis
 human, male: 1834
 virus-like particles, rat: 2000
 testis tumors, mouse: 73
- DIETHYLSTILBESTROL + TESTOSTERONE PROPIONATE
 implantation, uterine leiomyosarcoma, hamster:
 1833
- DIMETHACRINE (See Acridan, 9,9-dimethyl-10-
 dimethylaminopropyl-, hydrogen tartrate)
- DIMETHYL SULFOXIDE
 effect on dimethylbenzanthracene skin tumors,
 resistant mouse strain: 1079
- DIOXANE
 nasal cavity and liver tumors, rat: 1160
- 4-DIPHENYLAMINE
 bladder tumors, rabbit: 1850
- DIPHENYLMETHANE, 4,4'-DIAMINO-
 toxicity, rat: 1894
- DIPHENYLMETHANE, 3,3'-DICHLORO-4,4'-DIAMINO-
 liver and lung tumors, rat: 1894
- DISEASE OUTBREAKS
 leukemia clusters
 California (Los Angeles), children: 1700
 children, Wisconsin (Green Bay): 2093
 Europe, review: 2135
 Japan: 2597, 2598, 2599, 2600
 adults and children, Tokai district:
 1676
 measles, Tokyo and Yagawara. children:
 1675
 virus diseases and radiation exposure:
 2095
 multiple-case house, Georgia: 917
 New England: 1677
 time between case pairs, Connecticut: 2094
 reticulum cell sarcoma, leukosis- and
 lymphoma-free colony of Japanese quail,
 Hawaii (Honolulu): 2051

DISEASE TRANSMISSION

cellular
 hamster tumor (TM lymphoma), insect vector
 (*Aedes*): 555
 L₂C leukemia, guinea pig: 2634
 leukemia or lymphoma, dog: 2112
 cervix or prostate cancer, viral etiology,
 review: 576
 feline fibrosarcoma virus
 marmoset: 2504
 transplacental, kittens or puppies: 2392
 herpesvirus type 2, venereal, Texas (Houston):
 510
 human leukemia
 mouse: 2502
 primates (baboons or macaques), virus-like
 particles: 2503
 liver carcinoma, human, to mouse: 2502
 Lucké herpes-type virus, horizontal or vertical,
 frog: 2493
 mammary tumor virus
 effect of host genotype, mouse: 481
 high-tumor (IBA/Gf) to low-tumor (X/Gf)
 mouse strains, foster-nursing: 1642
 mouse leukemia viruses, mouse strains: 95,
 755, 2352
 Rous sarcoma virus
 dexamethasone-treated baboons: 457
 poultry farm to quail farm, USSR: 2382
 sarcoma virus, possible, sarcoma pts. and
 their relatives: 815, 1591
 serum antibodies to leukemic antigens, leukemia
 pts. and their relatives: 1969

DISTRIBUTION

aflatoxins
 birds: 2294
 mammals: 2294
 monkey or human: 1113
 rat: 668, 740, 1108, 1113
 benzpyrene
 dietary, meat and milk, cows: 2216
 rabbits, hens and cows: 2217
 effect of vehicle, rat or hamster: 1799,
 2201
 human: 1796
 mouse: 1528, 1794
 rat: 641
 beryllium oxides
 effect of particle properties, rodent: 2312
 dibenzpyrene
 mouse: 1170
 diethylnitrosamine
 rat: 1530
 dimethylbenzanthracene
 dermal mast cells, hairless strain mice:
 1520
 DNA binding, rat: 1801
 mammary gland, rat: 1212, 1826
 dimethylnitrosamine
 subcellular, mouse liver: 200
 fluorenylacetamide and derivative
 effect of germ-free status, rat: 433, 434
 gallium
 leukemic or nonleukemic AKR/J mice: 1775
 hydroxyanthranilic acid
 rat with/without hydroxyanthranilic acid-
 induced bladder tumor: 1474

DISTRIBUTION (contd.)

Moloney sarcoma virus
 newborn mouse: 1304
 nitroquinoline oxide
 mouse: 432
Tetrahymena pyriformis: 2275
 nucleic acids and nucleases
 Friend leukemia virus-infected mouse spleen:
 1306
²³⁹Pu
 effect of oophorectomy, rat: 2299
 4'-substituted dimethylaminoazobenzenes
 biliary metabolites, rat: 648
 sugar transport
 Harvey sarcoma virus-infected or -trans-
 formed cells: 2360
 transcellular glutamate migration
 cell membrane properties, normal or
 malignant liver cells, rat: 976
 urethan
 effect of partial hepatectomy, mouse: 2285
 DODECYL METHYL ETHER
 juvenile hormone activity and tumor induction,
Drosophila: 1194
 DUCTUS DEFERENS NEOPLASMS
 androgen- or estrogen-induced, hormone-inde-
 pendent variants, hamster: 1130
 DUST
 atmospheric
 analysis, benzpyrene, Switzerland, urban
 (Zurich) and rural: 2214
 benzpyrene-containing, stomach tumors, mouse:
 1791
 lung or stomach cancer, England and Wales:
 1660, 1661
 polynuclear hydrocarbons, analysis, method:
 1786
 beryllium oxides, toxicity (rodent) and lung
 tumors (rat): 2312
 carbon black
 benzpyrene-adsorbed, effect on benzpyrene
 uptake by lung, hamster: 2201
 effect on tumor cells or tobacco callus
 in vitro: 1124
 cerium hydroxide, combined with radon, lung
 tumors, rat: 2171
 coal, occupational exposure, chronic bronchitis,
 smoking, Germany: 1117
 occupational exposure
 asbestos needles in lungs: 680
 lung cancer, Scotland, smoking: 1659
 nasal cavity and sinus tumors, shoe
 manufacturing, England (Northamptonshire),
 snuff taking: 1658
 rubber, effect on tumor cells or tobacco
 callus in vitro: 1124
 silicon, occupational exposure, primary
 hemangioendothelial tumor of heart: 682
 soot from exhaust gas, benzpyrene content,
 Soviet aircraft of different types: 1480
 DYES AND STAINS
 acridine orange, skin tumors, mouse: 237
 Ponceau MX (food coloring), toxicity, liver,
 mouse: 609
 printing inks, s.c. sarcoma, mouse: 607
 starting material, liver or skin tumors,
 mouse or rat: 2272

DYES AND STAINS (contd.)

- trypan blue or toluidine blue, mutagenesis and effect on tumor incidence, Drosophila: 626

EAR DUCT NEOPLASMS

- induction
 - fluorenylacetamide, rat: 417
 - 5-nitrofur derivatives, rat: 417

EB VIRUS (See under Virus, herpes-type)

ELECTRICITY

- effect on rat tumor: 1750, 2181

EMBRYO (See also Teratogenesis)

- brain, effect of methyl nitrosourea, rat: 1876, 1879
- crustacean, effect of carcinogens: 1861
- genital ridge, transplantation, testicular teratoma, mouse: 1703
- kidney, effect of transplacental dimethylbenzanthracene, mouse: 2224

Encephalartos hildebrandtii FLOUR

- kidney tumors, rat: 405

ENDOCRINE ABLATION

adrenalectomy

- effect on
 - fluorenylacetamide liver tumors, mouse or rat: 424, 1843
 - Friend leukemia virus infection, mouse: 96

hypophysectomy

- effect on
 - dimethylbenzanthracene uptake, rat mammary gland: 1212
 - induced or transplanted rat hepatoma: 185, 424, 1534
 - thyroid tumor induction (low-iodine diet + ¹³¹I), rat: 2265

oophorectomy

- effect on
 - dimethylbenzanthracene tumor induction, animal: 708, 1212, 1811, 1820, 1822, 1824, 2231
 - DNA, hyperplastic alveolar mammary nodules, mouse: 1623
 - hydrazine lung carcinogenesis, mouse: 1498
 - liver and hepatoma growth, hepatoma-susceptibility genotype, mouse: 2619
 - methylcholanthrene s.c. tumors, mouse: 41
 - ²³⁹Pu distribution, rat: 2299
 - transplanted tumor, mouse: 1507, 2267
 - mammary tumor risk, dog: 969

orchiectomy

- effect on
 - benzpyrene-induced brain tumors, rat: 1094
 - dimethylaminoazobenzene tumors, rat: 2264
 - dimethylbenzanthracene tumors, hamster or rat: 696, 1076, 2264
 - fluorenyldiacetamide hepatoma, rat: 424
 - hydrazine lung carcinogenesis, mouse: 1498
 - liver and hepatoma growth, hepatoma-susceptibility genotype, mouse: 2619
 - methylcholanthrene tumors, mouse: 41, 2197

ENDOCRINE ABLATION (contd.)

- transplanted tumor, mouse: 1507, 2267
- pinealectomy
 - effect on chemical liver carcinogenesis, rat: 416

ENDOCRINE ORGAN NEOPLASMS

- multiple, familial polyadenomatosis syndromes, review: 565
- Type 2, syndrome, pathogenesis: 2651
- ²³⁹Pu-induced, rat: 2177

ENDOMETRIUM NEOPLASMS (See under Corpus uteri neoplasms)

ENDOTOXINS, BACTERIAL

- effect on methylcholanthrene tumors, rat or mouse: 1565, 2192
 - runtng syndrome, tumor induction, mouse: 1200
- ENGINE EXHAUST GASES (See also Air pollution and Petroleum and petroleum products)
- benzpyrene content
 - aircraft exhaust: 1480
 - automobile engines, fuel type and engine efficiency: 1481
 - diesel fuel combustion products, salt-drying method, benzpyrene content: 2210
 - rocket exhaust, beryllium-containing, toxicity (rodents) and lung tumors (rat): 2312
 - soil and plant benzpyrene contents, airport: 2212

ENVIRONMENTAL FACTORS

- altitude, effect on radiation carcinogenesis, mouse: 1749
- cancer epidemiology
 - India and other tropical nations, review: 1448
 - migrant populations, international: 1338
- cell cultures, medium pollution rates: 980
- coal-mining and textile-manufacturing areas, lung cancer, England and Wales: 1660
- exposure to non-industrial chemicals, bladder cancer, review: 570
- geographical variations
 - brain tumors, Denmark and U.S.: 1684
 - cancer epidemiology, Kenya (western) and Tanzania (northwestern): 2520
 - climate, rainfall and soil type, cancer epidemiology, U.S.: 1342, 1647
 - larynx cancer, Ukrainian SSR: 2534
 - leukemia, Japan: 2597, 2598, 2599, 2600
 - lip cancer, U.S.: 2530
 - stomach cancer, ethnic groups, Uzbekh SSR: 2547
 - Japan (Osaka and Nara prefectures): 2546
 - Utah: 2552
 - temperature, cancer mortality, U.S.: 1342
- g.i. cancer, Oklahoma, ethnic groups: 1648
- industrial and non-industrial regions of city (Hamburg, West Germany), cancer distribution: 1652
- isolation or crowding, effect on dimethylbenzanthracene mammary tumors, rat: 1070
- leukemia epidemiology, Europe, review: 2135
- liver cancer, international: 2561
- liver carcinogens, review: 2118
- lymphoma, Saudi Arabia (Dhahran): 2091
- nasopharynx cancer
 - Chinese and other Oriental populations, review: 1719

ENVIRONMENTAL FACTORS (contd.)

- South Vietnam: 330
 - nitrosamines, foods, review: 164
 - oropharynx cancer, U.S.: 1384
 - permissible carcinogen concentration limits: 736
 - population density, stomach cancer, England and Wales: 1661
 - salivary gland tumors, U.S.: 1663
 - seasons
 - acute leukemia, children, Maryland (Baltimore): 2590
 - Hodgkin's disease, Germany: 525, 2606
 - melanoma incidence, amphibian (*Triturus*): 628
 - solar activity, leukemia, Poland (Cracow): 1392
 - virus-positive kidney tumors, frogs, Minnesota: 2494
 - socioeconomic status and occupation, cervix or uterus cancer, Poland: 520
 - soil type and rainfall, cancer distribution, U.S.: 1647
 - stomach cancer (intestinal metaplasia type), Colombia (Cali), migrants: 1390
 - tropical climate, cancer epidemiology, India and other nations, review: 1448
 - urbanization
 - benzpyrene content of air-borne dust, Switzerland (Zurich): 2214
 - bladder cancer, tryptophan metabolism, Boston or Wisconsin: 70
 - bronchitis, Great Britain: 2535, 2536
 - bronchus cancer, East Germany: 527
 - cancer epidemiology, France: 2521
 - Poland: 2524
 - cervix or uterus cancer, Poland: 520
 - lung cancer, air pollution and smoking, Scotland: 2536
 - Poland: 529
 - stomach cancer, Rumania: 2515
 - testis tumors, Denmark: 936
 - tongue and lip cancer, Canada: 895
- ZYMES (See also Isoenzymes)
- acid phosphatase
 - mouse viral sarcoma: 1590
 - adenosine triphosphatase
 - avian myeloblastosis assay method: 464
 - viral sarcoma, mouse: 1590
 - aldolase
 - effect of carcinogens, rat liver: 1468, 1928
 - alkaline phosphatase
 - induced brain tumors, rat or mouse: 1051, 2283
 - thymic lymphoma induced by 6-mercaptopurine (or virus derived from the tumor) or dimethylbenzanthracene, mouse: 2389
 - aminoacyl-RNA synthetase
 - effect of benzanthrone and phenanthrene compounds, cell-free system: 1184
 - aminopyrine demethylase
 - effect of nickel carbonyl, rat liver or lung: 2310
 - arginase
 - nickel sulfide-induced rhabdomyosarcoma, rat: 1177

ENZYMES (contd.)

- antitumor (L-asparaginase)
 - effect on Rauscher viral leukemia, mouse: 1579
- aryl hydrocarbon hydroxylase
 - effect of benzanthrone, normal or transformed cells: 381, 647
 - placenta, smoking, human: 685
- aspartate transcarbamylase
 - dimethylbenzanthracene mammary tumors, rat: 2228
- atypical, familial polyposis of colon with malignant transformation: 2103
- benzpyrene hydroxylase
 - effect of aflatoxin or benzpyrene, rat liver microsomes: 1116
 - trace metals and asbestos, mouse lung: 1764
- methylcholanthrene induction, rat liver or hepatoma: 1904
- strain differences, mouse liver: 2205
- butyl-N-4-butanolnitrosamine-induced bladder tumors, rat: 1536
- cadmium-induced s.c. sarcoma, rat: 235
- catalase
 - liver, normal and tumor-bearing rat: 1341, 2652
- collagen:galactosyl transferase
 - SV40- or polyoma-transformed cells: 2019
- dehydrogenases
 - estrogen-induced kidney tumor, hamster: 72
 - growing and regressing viral sarcoma, mouse: 1590
 - hamster cheek pouch or human oral tumors: 373
 - Rous sarcoma virus-transformed or Rous-associated virus-infected cells: 1588
- dibutylnitrosamine bladder tumors, rat: 244
- diethylnitrosamine hepatoma, rat: 195
- dimethylhydrazine-induced duodenal tumors, rat: 1497
- DNA polymerase
 - relation to growth rate, rat liver or hepatoma: 140
- DNase
 - effect of carcinogens, cell-free system: 612
 - Friend leukemia virus-infected mouse spleen: 765, 1571
- DOPA oxidase
 - melanocytes of methylcholanthrene- or dimethylbenzanthracene-induced skin tumors, mouse: 1067
- endonuclease
 - effect on SV40 DNA: 2506
 - polyoma-transformed hamster cells: 2060
- esterases
 - hamster cheek pouch or human oral tumors: 373
 - methylcholanthrene-induced brain sarcoma, mouse: 1051
 - serum, aflatoxin-induced hepatoma, rat: 2292
- fluorenylacetamide liver tumor, rat: 1846
- fructose phosphate aldolase
 - diethylnitrosamine liver damage, rat: 1148

ENZYMES (contd.)

- β -glucuronyltransferase
 - induced or transplanted hepatoma, rat: 1902
- glucose phosphorylation
 - induced liver tumors, rat: 1928, 2261
- glutamic-oxaloacetic transaminase
 - isozymes, serum, human cancer: 344
- glutathionase
 - transplanted or induced hepatoma, rat: 652
- hydroxyacetylaminofluorene sulfotransferase
 - species difference, liver carcinogen susceptibility, rodent: 1550
- hydrolases
 - methylnitrosourea-induced brain tumors, rabbit: 1519
- lactate dehydrogenase
 - isoenzymes, carcinogen-transformed hamster embryo cells: 1561
 - distribution, female genital cancer, Poland: 550, 551
 - effect of carcinogen and cupric acetate, rat: 2260
 - dimethylbenzanthracene, human fibroblasts: 211
 - mammary tumor, rat: 55
 - rat tumor cells and transforming rat lung cells: 553
- metabolism, breast cancer or fibrocystic disease: 938
- methylnitrosourea-induced brain tumors, rabbit or rat: 242, 254, 631
- microsomal
 - effect of
 - aflatoxin, animal liver: 81
 - benzanthracene, hamster embryo cells: 647, 1828
 - methylcholanthrene, animal: 1903, 2326
 - liver, biliary benzpyrene excretion, rat: 2324
- mitochondrial, effect of Friend and Rauscher leukemia virus, mouse spleen and liver: 1634
- monoamine oxidase or histaminase
 - effect of benzdine and related compounds, rat: 2232
- muramidase
 - mineral oil + androgen-induced leukemia, mouse: 406
- mitrosamine breakdown in vitro, rat liver or kidney: 644
- oxidoreductases
 - methylnitrosourea-induced brain tumors, rabbit: 1519
- pathogenesis of human leukemia, review: 1438
- phenyldimethyltriazene- or methylnitrosourea-induced brain tumors, rat: 2269, 2270
- phosphomonoesterase
 - premalignant and malignant intestinal polyposis: 964
- polynucleotide ligase
 - SV40- or polyoma virus-infected cells: 318
- pyruvate kinase
 - rat tumor cells and transforming rat lung cells: 553
- relationship to growth rate, dimethylbenzanthracene mammary tumors, rat: 1825

ENZYMES (contd.)

- ribonucleotide reductase
 - Yaba virus-induced monkey tumors: 125
 - RNA-dependent DNA polymerase
 - Rous sarcoma or Rauscher leukemia virus particles: 1583, 2388
 - RNA-dependent RNA polymerase
 - virus-induced avian myeloblastosis: 1230
 - RNase
 - Friend leukemia virus-infected mouse spleen 765, 1571
 - and inhibitor, liver and spleen, ascites mouse leukemia: 343
 - succinate dehydrogenase
 - dimethylbenzanthracene cheek pouch tumors, hamster: 695
 - tetrahydrofolate dehydrogenase
 - virus-induced leukemias, mouse: 2350
 - thymidine kinase
 - adenovirus-5 or -12-infected cells: 836
 - induction, effect of temperature, SV40-infected cells: 874
 - polyoma virus-induced hamster tumor cells: 1608
 - thymidine triphosphate pathway
 - methyl dimethylaminoazobenzene liver tumors, rat: 1142
 - transfer RNA methylase
 - GA (Marek's disease-associated) virus-induced liver tumor, chick: 1319
 - mouse or rat mammary tumors: 2647
 - trypsin esterase
 - binding, radiation-leukemia protection factor, sheep spleen or serum extracts: 1035
 - tryptophan oxygenase
 - hormone induction, effect of carcinogens, animal: 197, 1933
 - zoxazolamine hydrolase
 - effect of benzpyrene or tobacco smoke, hamster or rat liver: 180
- EPIDEMIOLOGY
- all tumors
 - anesthesiologists, U.S. and Canada: 888
 - Armenian SSR (Chuvash): 2069
 - Australia, association with other diseases, aged men: 892
 - Brazil (São Paulo), children: 1681
 - Bulgaria, children: 1378
 - Canada: 894
 - Colombia (Cartagena): 329
 - Congo (Brazzaville): 2514
 - Czechoslovakia (České Budějovice district): 1376
 - Dominican Republic: 1650
 - East Africa: 885
 - Finland: 1380
 - France: 328
 - air pollution: 2521
 - occupational groups: 2522
 - genetic factors, diabetes mellitus and cancer susceptibility: 541
 - Germany
 - aged, Magdeburg: 1372
 - diabetes mellitus, Stralsund: 891
 - industrial and non-industrial areas, Hamburg: 1652

DEMOLOGY (contd.)

high-risk diseases, children, review: 2137
 Hong Kong (Chinese): 1382
 Hungary, infants and children: 1348
 India
 ethnic groups, Bombay: 2066, 2067
 review: 1448
 international (14 nations): 2513
 Israel: 530, 879
 ethnic groups: 1651
 Italy
 age factors, Milan: 2096
 high-mortality rate area (Spoleto): 326
 trace metals in drinking water, Pesaro: 2072
 Jamaica, children: 884
 Kenya (western) and Tanzania (northwestern), geographical variations: 2520
 kidney transplantation with immunosuppression: 2087
 Massachusetts, diabetes mellitus: 2519
 methods of calculation: 1445, 1649
 migrant populations, international: 1338
 New Jersey and New York, occupational asbestos exposure: 2071
 New York (Kings County), appendectomy and/or tonsillectomy: 2586
 Nigeria (Ilesha township): 2523
 occupational radiation exposure: 1755
 Poland: 2524, 2525
 prevention and competitive risks, review: 1444
 Rumania: 2515, 2516
 sex ratio, England/Wales and western Europe: 1389
 smoking: 2070, 2071
 socioeconomic status: 2070
 South Africa
 doctors and dentists, smoking, ethnic groups: 1655
 ethnic groups, Johannesburg: 2068
 South Korea: 944
 Switzerland: 128, 531, 2526
 tropical nations, review: 1448
 U.S.
 adolescents and children: 890
 chemists: 933
 children vaccinated with SV40-containing polio vaccine: 316
 geographical variations, climate, rainfall and soil type: 1342, 1647
 newborn infants: 2518
 USSR, urban: 2517
 Washington (Seattle), aged: 893
 asbestos exposure
 Michigan (Detroit and Lower Peninsula): 1102
 review: 1018
 benign fibroadenoma of breast
 oral contraceptives, Texas (Houston): 1806
 biliary tract cancer
 Germany (Göttingen-Weende): 1360
 bladder cancer
 artificial sweeteners including cyclamates, U.S.: 2544
 benzidine or β -naphthylamine exposure, U.S.: 545

EPIDEMIOLOGY (contd.)

phenacetin abuse, Sweden: 1123, 2545
 review: 532
 rubber manufacturing, Britain: 544, 927, 1119
 smoking, U.S.: 1337
 urinary tryptophan metabolites, Boston or Wisconsin: 70
 bone tumors
 age factors, skeletal growth rate: 2089
 children, U.S., ethnic groups: 1682
 East Germany: 2090
 radiation exposure, Hiroshima/Nagasaki: 1027
 brain tumors
 geographical variations, Denmark and U.S.: 1684
 Minnesota: 2579, 2580
 Poland (Cracow), temporal fluctuations: 2582
 review: 992
 South Africa (Transvaal), ethnic groups: 2581
 breast cancer: 335, 912, 2563
 age factors, Germany (Berlin): 2080
 international: 1388
 Canada: 894
 contraceptives, review: 2, 557
 England and Africa (Nigeria and Uganda), comparison of malignancy, genetic factors: 2562
 environmental temperature, geographical variations, U.S.: 1343
 Greece (Athens): 2075
 hormone metabolism, review: 583, 1724, 1725
 identification of high-risk groups, review: 582
 infants and children, Canada (Ontario): 1346
 irradiated postpartum mastitis, New York (upstate): 23
 Japan (Tokyo): 2566
 male, Finland: 1379
 Klinefelter's syndrome: 1400
 Massachusetts (Boston): 1356
 Minnesota (Minneapolis): 1344
 New York City: 2564
 Oklahoma, ethnic groups: 1353
 reproductive histories and lactation, international: 1356, 1385, 2079, 2565, 2566, 2567
 review: 532, 1723
 risk of second primary tumor, Connecticut: 909
 Taiwan: 2567
 Utah: 1687
 Wales (southern): 1385
 bronchiolo-alveolar carcinoma
 Finland (Helsinki): 903
 bronchus cancer
 East Germany, environmental factors: 527, 2543
 smoking: 526, 2543
 (Gliwice), women: 535
 Burkitt lymphoma
 Japan and Okinawa: 1671
 Kenya (western) and Tanzania (northwestern): 2520

EPIDEMIOLOGY (contd.)

- reovirus Type 3 and Epstein-Barr virus, review: 2138
- review: 355
- serum EB virus antibodies, children with tumor (Africa) and normal subjects: 509
- sickle cell trait genotype, Uganda (Kampala): 2609
- Uganda (West Nile District)
 - clustering: 133
 - malaria epidemiology: 878
- carcinoma of gastric stump
 - malignant transformation risk, Hungary (Pecs) or Poland (Lublin): 358, 359
- cervix cancer
 - Canada: 894, 2569, 2570
 - contraceptives, Czechoslovakia: 911
 - early lesions, methods: 519
 - Georgia (Atlanta), serum herpesvirus-1 or -2 antibodies: 2576
 - Germany, diabetes and hormonal factors: 1688, 1690
 - hormonal or mechanical contraceptives, New York City: 1387
 - India, ethnic groups, Bhopal: 2573
 - southern: 1363
 - Japan, hormonal factors: 1690
 - intrauterine contraceptive devices: 1455
 - Kentucky (Louisville): 135, 2571
 - microinvasive, Ohio (Cleveland): 1361
 - Natal, ethnic groups: 1689
 - New Zealand, ethnic groups: 2572
 - Poland: 520, 910, 2624
 - pregnancy, Oklahoma (Oklahoma City): 906
 - Pennsylvania (Philadelphia): 907
 - Puerto Rico, tubal-ligation sterilization: 2574
 - reproductive histories, U.S.: 2568
 - review: 356, 1721
 - serum herpesvirus type 2 antibodies, Texas (Houston): 510
 - South Africa (Cape Town), ethnic groups: 908
 - USSR (Krivoi Rog), methods: 2575
 - Utah: 1352
 - viral etiology, review: 576
- cholangiocarcinoma of liver
 - Switzerland (Zurich): 129
- choriocarcinoma and related diseases
 - Australia (Sydney): 1367
 - Iraq: 1366
- chromosomal aberrations
 - atomic radiation exposure, Japan: 1757
 - cancer pts. and normal population: 956
- chronic toxic symptoms
 - occupational arsenic exposure, Poland (Zloty Stok): 1118
- colon/rectum cancer
 - California (Los Angeles), ethnic groups: 2556
 - Denmark (Copenhagen): 898
 - Jamaica: 2557, 2622
 - single- or multiple-"hit" models: 2085, 2086
 - Tennessee (Nashville), ethnic groups: 2555
- connective tissue tumors
 - East Germany: 2090

EPIDEMIOLOGY (contd.)

- Mexico City, children: 1362
- endometrial cancer
 - hormonal status: 1357, 1431
 - identification of high-risk groups, estrogen metabolism: 1136
- esophagus cancer
 - central Africa (Zambia and Malawi), alcohol beverages: 1122
 - Ceylon, betel chewing: 2081
 - France, alcohol consumption, geographical distribution: 2081
 - Jamaica and Western Australia, dietary factors: 2533
 - Kenya (western): 1369
 - smoking and dietary factors, Puerto Rico: 932
 - South Africa, ethnic groups, environmental factors: 928, 1121, 1386, 2068
 - U.S. (nonwhite) and Africa (high- or low-cancer nations), smoking and occupation: 1698
- extrapulmonary tumors
 - TB, USSR (Moscow): 2073
- Fallopian tube cancer
 - New York (Long Island): 1358
- familial cancer
 - age-, sex- and site-related patterns: 1679
 - multiple tumor types including neuroblastoma: 2088
- familial polyposis of colon
 - risk of malignant transformation: 2558, 2672
- female genital cancer
 - Connecticut, risk of second primary tumors: 909
 - contraceptives, review (book): 557
 - genetic factors (serum LDH fractions, blood groups and PTC tasting), Poland: 550, 551
 - Germany (Giessen), diabetes and hormonal factors: 1688
 - New York (upstate): 2577
 - Oklahoma, ethnic groups: 1353
 - USSR (Kirovabad), ethnic groups: 2078
- gallbladder cancer
 - Finland, cholelithiasis: 899
 - Germany, cholelithiasis, sex difference: 130
 - Göttingen-Weende: 1360
 - Poland (Warsaw), cholecystitis: 1350
- g.i. cancer
 - environmental temperature, geographical variations, U.S.: 1343
 - Kenya (western) and Tanzania (northwestern): 2520
 - Natal (Durban), betel chewing, ethnic groups: 1656
 - Oklahoma, ethnic groups and environmental factors: 1648
 - risk, effect of appendectomy, West Germany: 2587
 - smoking, Poland: 542
- head and neck tumors
 - children, Sweden (Malmö): 2583
 - sunlight, Sweden: 2529

EPIDEMIOLOGY (contd.)

Hodgkin's disease
 hepatitis-associated (Australia) antigen
 distribution: 2591
 Israel, ethnic groups: 1696, 1697
 relationship to multiple sclerosis, review:
 2139
 review: 532, 1726
 seasonal variations, Germany (Göttingen):
 525
 West Germany: 2606, 2607
 worldwide: 524, 1726
 intestinal cancer
 dietary protein, international: 1432
 risk of multiple primary cancer: 1359
 Kaposi's sarcoma
 Nigeria: 1371
 Tanzania (mainland): 134
 kidney cancer
 phenacetin abuse, Sweden: 1123, 2545
 review: 581
 smoking, U.S.: 1337
 larynx cancer
 blood groups, East Germany: 1670
 smoking and occupation, Czechoslovakia:
 881
 Poland (Cracow): 528
 Ukrainian SSR (Kirovograd), occupation and
 geographical variations: 2534
 leukemia
 Australia, rheumatic disorders: 2625
 California (Los Angeles), children:
 1345, 1700
 Canada, children, Saskatchewan: 1377
 children, perinatal and congenital, twins,
 review: 2136
 clustering, adults and children: 126, 917,
 1675, 1676, 1677, 1700, 2093, 2094, 2095
 congenital chromosomal anomalies, review:
 1733
 Connecticut, clustering: 2094
 environmental factors, Europe, review:
 2135
 familial
 cases and review: 1447
 Japan: 2605
 multiple-case family (7 generations):
 1678
 Nebraska: 1333
 France, reproductive history: 2594
 genetic factors: 918
 Georgia, ethnic groups, Atlanta: 2593
 multiple-case house: 917
 haptoglobin and Gc group genotype: 1397,
 2595
 hepatitis-associated (Australia) antigen
 distribution: 2591
 high-risk groups, chromosomal defects,
 review: 585
 Japan: 2596
 age factors: 1674
 children, clustering, virus diseases:
 126, 1675, 1676
 clustering, adults or children: 126,
 1675, 1676, 2095
 correlation with other tumors:
 2601

EPIDEMIOLOGY (contd.)

diagnostic or therapeutic radiation
 exposure: 18, 19, 561, 2166, 2167,
 2168, 2604
 familial: 2605
 geographical variations: 2597, 2598,
 2599, 2600
 Hiroshima and Nagasaki: 19, 1672,
 2602, 2603
 Maryland (Baltimore), children, seasonal
 onset: 2590
 Massachusetts, mongolism: 1335
 New England, clustering: 1677
 New York, asbestosis: 1763
 Poland
 bovine leukosis areas (Zlatow district):
 1967
 dermatoglyphic abnormalities: 916, 1391
 Gc blood groups: 1397
 seasonal solar activity, Cracow: 1392
 review: 586, 1016
 U.S. metropolitan areas, ethnic groups
 (Jews, Russians and Poles): 2592
 viral etiology, review: 578
 Wisconsin (Green Bay), children, congenital
 defects, clustering: 2093
 life expectancy
 smoking, U.S. men: 900
 lip cancer
 environmental factors (including smoking),
 U.S.: 2530
 Italy (Catanzaro and Cosenza Provinces):
 1668
 liver tumors
 Africa, dietary pyridoxine deficiency: 970
 Bulgaria (southeastern): 522
 Congo (Brazzaville): 2514
 dietary carcinogens, review: 1014
 Ethiopia (Addis Ababa), dietary factors
 and folk medicines: 2084
 international, environmental factors
 (chemical and biological): 2561
 Japan, cirrhosis and alcohol consumption:
 2560
 Hiroshima/Nagasaki: 2559
 Switzerland (Zurich), cirrhosis: 129
 Uganda: 1374
 lung cancer
 air pollution: 902, 1657, 1659, 1699,
 2537, 2538, 2543
 review: 574
 California (San Diego), smoking, sex
 difference: 2541
 Canada: 894
 diabetic or nondiabetic men: 541
 East Germany, air pollution and smoking:
 2543
 exposure to solid fuels, international:
 179
 Hungary (Szeged), smoking: 1654
 Iceland, smoking: 1653
 Italy: 327, 994
 smoking: 325
 Japan (cities), air pollution and smoking:
 1657, 2538
 occupational pneumoconiosis with/without
 asbestosis: 2320, 2321

EPIDEMIOLOGY (contd.)

- occupational arsenic exposure, air pollution: 1699
- Poland, urban and rural: 529
- review: 532, 994
- Scotland, occupation, smoking and air pollution: 1659, 2536
- smoking: 128, 179, 325, 901, 904, 928, 1337, 1653, 1654, 1655, 1657, 1659, 1748, 2536, 2538, 2539, 2540, 2541, 2542, 2543
- Jews, Montreal: 2539
- Pittsburgh: 2540
- smoking, review: 166, 569, 574, 1024, 1714, 1715
- South Africa
 - doctors and dentists, smoking, ethnic groups: 1655
 - environmental carcinogens, ethnic groups: 928
 - ethnic groups, smoking: 901, 928, 2542
- Switzerland, smoking: 128
- TB
 - cancer risk, males: 127
 - treatment (pneumothorax), radiation and smoking: 1748
 - USSR (Moscow): 2073
- U.S., smoking: 1337
- Utah: 1351
- Wales (Swansea), ABO and Rh blood groups, smoking: 904
- West Germany, appendectomy: 2587
- lymphoma
 - associated high-risk immunity disorders, review: 585
 - Epstein-Barr virus-positive: 1255
 - Iran: 2092
 - Israel, children, ethnic groups: 2610
 - Jamaica: 2608
 - Nebraska, familial: 1333
 - New York, asbestosis: 1763
 - Ohio (Cincinnati), hydantoin anticonvulsants: 1909
 - Poland, bovine leukosis area (Zlatow district): 1967
 - review: 1016
 - Saudi Arabia (Dhahran), environmental factors: 2091
 - West Germany: 2607
- melanoma
 - Australia, sun exposure: 558, 1381
 - England and Wales, sex difference: 1683
 - familial incidence: 533
 - Nigeria: 1667
 - Switzerland: 2076
 - U.S., age factors: 2528
- mesenchymal tumors of thyroid
 - Italy: 913
- mouth cancer
 - Canada, comparison with other nations: 895
 - India, tobacco use, ethnic groups: 935, 2531
 - methods, review: 990
 - Papua/New Guinea, betel chewing: 693, 2532
 - Puerto Rico, smoking and dietary factors: 932

EPIDEMIOLOGY (contd.)

- U.S..environmental factors, ethnic groups: 1384
 - smoking: 1337
- multiple primary tumors
 - risk, stomach or intestinal cancer: 1359
- Sweden (Malmö): 1664
- upper g.i. or respiratory tract, smoking: 931
- West Virginia: 1354
- myeloma
 - Japan, myeloma globulin types, comparison with New York (white and Negro) group: 915
 - Jamaica: 132
 - Minnesota (Olmsted County): 1349
 - review: 14
- nasal sinus tumors
 - dust exposure (shoe manufacturing, bakers' flour) and snuff, England (Northamptonshire): 1658
- nasopharynx cancer
 - Chinese, California: 2075
 - review: 1719
 - genetic and environmental factors, review: 568
 - Japan and Taiwan: 2038
- East Africa, EB virus antibodies: 523
- Hong Kong (Chinese)
 - EB virus antibodies: 523, 825
 - possible genetic susceptibility to tumor virus: 825
- sinapylaldehyde exposure, international, review: 1004
- South Vietnam, environmental and genetic factors: 330
- neuroblastoma
 - children, Scotland, U.S. and Canada: 1685
- non-malignant respiratory diseases
 - air pollution, data evaluation methods: 2537
 - Germany, coal miners, smoking: 1117
 - Great Britain (including Scotland), air pollution and smoking: 2535, 2536
 - Japan (Tokyo), air pollution and smoking: 1657
 - Poland, occupational exposure to tobacco: 172
- oropharynx cancer
 - Poland (Cracow): 528
- ovarian cancer
 - New York (upstate): 2577
- pancreas cancer
 - diabetes, Scotland (northeastern): 1666
 - Germany (Heidelberg), chronic pancreatic diseases: 521
- phagedenic ulcer with malignant transformation
 - Senegal: 332
- pharynx cancer
 - smoking and dietary factors, Puerto Rico: 932
 - U.S., environmental factors and ethnic groups: 1384
- pleural mesothelioma
 - asbestos exposure, West Germany (Hamburg): 1370

EPIDEMIOLOGY (contd.)

- prostate cancer
 - Oklahoma, ethnic groups: 1353
 - viral etiology, review: 576
- respiratory cancer
 - Italy (Genoa): 905
 - U.S.
 - geographical variations, climate: 1343
 - occupational arsenic exposure: 926
 - smoking: 1337
- rhabdomyosarcoma
 - children, familial cancer syndrome, U.S.: 1334
- salivary gland tumors
 - Sweden (Stockholm): 2584
 - U.S., environmental factors: 1663
- second primary tumors
 - associated with chronic lymphatic leukemia: 882
 - risk, New York: 1665
 - women with salivary gland tumors: 338
- secondary malignant tumors
 - risk, nevus sebaceus of skin: 2527
- serum antibodies
 - adeno-associated viruses, cancer pts.: 2589
- adenovirus
 - human cancer: 834, 2588
 - Japan: 304
 - nasopharynx cancer, Hong Kong: 825
- Epstein-Barr virus
 - cancer pts.
 - Asia (Japan, Hong Kong or Taiwan): 523, 825, 925, 2038
 - East Africa: 509, 523
 - West Germany (Essen): 2037
 - normal subjects
 - Africa and other regions: 509, 523
 - Japan (Akita Prefecture): 296
 - U.S., young adults: 1256
- herpesvirus Type 2, cervix cancer: 510, 2043
- SV40 or Rous sarcoma virus, human cancer, Japan: 304
- serum α -fetoprotein
 - liver tumors or embryonal carcinoma of testis, review: 2134
- skin cancer
 - Germany (Giessen), age factors: 1365
 - head and trunk, Sweden, sunlight: 2529
 - India (Saurashtra): 1364
 - Minnesota: 1355
 - Nigeria: 1667
 - occupational, Britain: 889
- small intestine tumors
 - Japan: 2554
 - Michigan (Detroit): 2553
- solid tumors
 - children, Japan (Nagoya): 1347
 - twins, California: 1680
- ⁹⁰Sr levels
 - bones and teeth, USSR (all ages): 1453
- stomach cancer
 - air pollution, bioassay method: 1791
 - Armenian SSR (Yakutsk): 2548
 - Colombia (Cali), ethnic groups: 1390
 - dietary carcinogens, review: 1014
 - protein, international: 1432

EPIDEMIOLOGY (contd.)

- England and Wales, air pollution and occupational groups: 1661
 - Iceland, dietary factors: 2083
 - Japan
 - air pollution and smoking, Tokyo: 1657
 - geographical variations, Osaka and Nara prefectures: 2546
 - stomach ulcer: 1662
 - Minnesota (Minneapolis), pernicious anemia: 2551
 - Poland: 897, 1373, 1375, 2550, 2623
 - review: 532
 - risk of multiple primary cancer: 1359
 - two-hit and multiple-hit theories of carcinogenesis, mathematical models: 896
 - Utah, geographical variations: 2552
 - Uzbekh SSR, geographical variations, ethnic groups: 2547
 - Yugoslavia, geographical variations: 2549
 - testis tumors
 - Denmark, urban and rural: 936
 - Finland: 2578
 - thyroid cancer
 - Hawaii (Oahu): 2074
 - Israel: 883
 - Minnesota (Olmsted County; Rochester): 887
 - radiation exposure, Japan (Hiroshima/Nagasaki): 930
 - New York (Rochester): 2173
 - review: 584
 - South Korea: 1686
 - Switzerland (Lausanne): 2585
 - world, review: 2133
 - urinary tryptophan metabolites
 - dietary factors, Uganda: 1368
 - uterus cancer
 - Germany (Giessen), diabetes and hormonal factors: 1688, 1690
 - Kentucky (Louisville): 2571
 - Japan (Osaka), hormonal factors: 1690
 - Ohio (Lucas County), review: 2071
 - Poland, urban and rural: 520
- EPIDEMIOLOGY, VETERINARY
- adrenal tumors, high-tumor strain of Syrian hamsters: 2097
 - all tumors, dogs, USSR (Moscow): 2098
 - bovine leukosis, association with human leukemia/lymphoma, Poland (Zlatow district): 1967
 - latent SV40 or foamy virus infection, primate colony: 1276
 - leukemia, role of hairless (hr) gene, mouse: 919
 - Lucké renal adenocarcinomas, frogs, Minnesota, North Dakota and Louisiana: 2494
 - lymphoma, farm animals, U.S.: 1691
 - parainfluenza-like virus infection, squirrels (Britain), hamster tumor induction: 1299
 - reticulum cell sarcoma, leukosis- and lymphoma-free colony of Japanese quail, Hawaii (Honolulu): 2051
 - Rous sarcoma virus antibodies, domestic and wild birds, USSR: 2382
 - skin papillomas, fish, San Francisco Bay, species specificity and water pollution: 534

EPIDEMIOLOGY, VETERINARY (contd.)

- spontaneous mammary and other tumors, virus-positive or virus-free mouse strains: 554, 983
- spontaneous tumors, colony of *Myiostomys albicaudatus* (African white-tailed rats): 1692
- testis tumors, possible genetic or viral influence, Mexican axolotl (*Ambystoma mexicanum*): 2650
- thyroid cancer and parathyroid hyperplasia, strain differences, rat: 1433

EPOXIDES

- mechanism of action, animal, review: 1001

EPOXY COMPOUNDS

- effect on crustacean eggs: 1861

EPSILON-AMINOCAPROIC ACID

- effect on transplanted tumors, mouse: 2302

EPSTEIN-BARR VIRUS (See under Virus, herpes-type)

EQUINE PAPILLOMA VIRUS (See under Virus, papova)

ESOPHAGUS NEOPLASMS

- cell growth kinetics, measurement method: 2614
- epidemiology
 - Australia and Jamaica, comparison, dietary factors: 2533
 - Ceylon, betel chewing: 2081
 - France, alcohol consumption, geographical distribution: 2081
 - Kenya (western): 1369, 2520
 - Malawi, alcoholic beverages: 1122
 - Natal (Durban), ethnic groups, betel chewing: 1656
 - Poland, smoking: 542
 - Puerto Rico, smoking and dietary factors: 932
 - review: 532
 - South Africa, environmental factors, ethnic groups: 928, 1121
 - ethnic groups: 1386, 2068
 - Tanzania (northwestern): 2520
 - U.S. (nonwhite) and Africa (high- or low-cancer nations), smoking and occupation: 1698
 - Zambia, alcoholic beverages: 1122
- familial, siblings: 1669
- gastrectomy or gastroenterostomy: 1045
- induction
 - dibutyl nitrosamine, mouse: 248
 - ethylbutyl nitrosamine, rat: 1535
 - nitrosomethylaniline, rat: 231
 - nitrosopiperidine, mouse: 67
- malignant transformation
 - of achalasia of cardia or chemical stricture: 360, 1457, 1741, 2159, 2160
 - of marginal or pharyngoesophageal diverticulum: 1000, 2669, 2670
 - of megaesophagus: 961
- radiation cure of tracheal cancer: 593

ESTRADIOL

- binding, benign or malignant human breast tumors: 1505
- effect on
 - dimethylbenzanthracene mammary tumors, rat: 1821, 1824
 - transplanted tumor, sex difference, mouse: 1507

ESTRADIOL (contd.)

- leiomyosarcoma of ductus deferens, hormone-independent variants, hamster: 1130
- mammary nodule induction, effect of mammary tumor or nodule-inducing virus, mouse: 286, 820, 821
- metabolism, high-endometrial cancer-risk women: 1136
- osteoma of skull, mouse: 718

ESTRADIOL BENZOATE

- cervix or skin tumors, rat: 707
- effect on transplantable mammary tumors, mouse: 2267

ESTRADIOL DIPROPIONATE

- pituitary adenoma, prolactin- and growth hormone-secreting cell types, rat: 1501

ESTRADIOL, ETHYNYL-

- effect on dimethylbenzanthracene induction of cervix cancer, mouse: 1128

ESTRADIOL VALERATE

- pituitary tumors, mouse: 1129

ESTROGENS

- binding, mouse mammary tumor: 155
- carcinogenic activity, role of pituitary-adrenal system, review: 2120
- effect on
 - adenovirus-12 tumors, hamster: 122
 - dimethylbenzanthracene cheek pouch tumors, intact or orchiectomized hamster: 696
 - methylnitrosourea-induced brain tumors, rat: 2284
 - mouse mammary tumor virus: 116
 - spontaneous or adenovirus-induced transformation, hamster cells: 2002
- metabolism, breast cancer, review: 1, 1724
- women with larynx cancer: 1835
- synthesis, testicular tumor, mouse with mammary tumor: 152

ESTRONE

- pituitary tumors, plasma prolactin, male rat: 728

ESTRUS CYCLE

- effect on
 - cell growth kinetics, mouse tumor: 137
 - rat mammary gland: 2616

ETHANOL

- tumor promotion, hamster cheek pouch: 1802

ETHER, BIS(CHLOROMETHYL)-

- lung tumors, mouse: 676
- skin tumors, mouse: 419

ETHER, CHLOROMETHYL METHYL-

- lung tumors, mouse: 676

ETHERS, HALOGENATED

- mechanism of action, animal, review: 1001
- skin tumors, mouse: 419

ETHIONINE

- effect on
 - crustacean eggs: 1861
 - dimethylbenzanthracene ovarian tumors, mouse: 218
 - liver RNA, rat: 201
 - m-toluenediamine liver tumors, rat: 2235
 - liver tumors, rat: 1144, 1173, 1847
- ETHNIC GROUPS
 - bone tumors
 - children, U.S.: 1682

ETHNIC GROUPS (contd.)

brain tumors
 Minnesota: 2579
 South Africa (Transvaal): 2581
 breast cancer
 Oklahoma: 1353
 review: 1723
 cancer epidemiology
 India (Bombay), Hindus and Parsis: 2066, 2067
 Israel: 1651
 migrant populations, international: 1338
 South Africa: 2068
 doctors and dentists, smoking: 1655
 cervix cancer
 India (Bhopal): 2573
 Kentucky (Louisville): 2571
 Natal: 1689
 New Zealand: 2572
 review: 1721
 South Africa (Cape Town): 908
 colon/rectum cancer
 California (Los Angeles): 2556
 Tennessee (Nashville): 2555
 esophagus cancer
 South Africa: 928, 1121, 1386
 U.S. (nonwhite) and Africa (high- or low-incidence regions): 1698
 female genital cancer
 Oklahoma: 1353
 USSR (Kirovabad): 2078
 g.i. cancer
 environmental factors, Oklahoma: 1648
 Natal (Durban), betel chewing: 1656
 Hodgkin's disease
 Israel: 1696, 1697
 leukemia
 aged, Georgia (Atlanta): 2593
 U.S. metropolitan areas: 2592
 lip cancer
 U.S.: 2530
 lung cancer
 smoking
 Montreal: 2539
 Pittsburgh: 2540
 South Africa: 901, 928, 2542
 lymphoma
 children, Israel: 2610
 mouth cancer
 France and Canada (Quebec): 895
 nasopharynx cancer
 Chinese, California: 2075
 review: 1719
 Hong Kong: 825
 oral and pharyngeal cancer
 tobacco chewing, India (Madhya Pradesh): 2531
 U.S.: 1384
 prostate cancer
 Oklahoma: 1353
 stomach cancer
 intestinal metaplasia type, migrants,
 Colombia (Cali): 1390
 Uzbekh SSR: 2547
 EYE NEOPLASMS

EYE NEOPLASMS (contd.)

retinoblastoma, dermatoglyphic abnormalities: 2108

FARNESYL METHYL ETHER

juvenile hormone activity and tumor induction, *Drosophila*: 1194

FATS (See also Lipids and Oils, edible)

dietary, hepatoma, mouse or rat: 250, 673
 heated, s.c. or g.i. tumors, rat: 241
 or unheated, effect on methylcholanthrene g.i. tumors, guinea pig: 1899
 margarine or chocolate, carcinogen content, processing methods, Germany: 604

FATTY ACIDS

deficiency, effect on fluorenylacetamide liver tumors, rat: 1844
 s.c. sarcoma, mouse: 1494

FATTY ACIDS, CYCLOPROPENOID (See also under Cyclopropene compounds)

effect on aflatoxin carcinogenesis, rat or trout: 362, 2330

FEEDS, ANIMAL

aflatoxin content
 detection method: 1918
 products of African or French origin: 2296
 toxicity, review: 572
 benzpyrene-containing
 benzpyrene distribution in meat and milk, cows: 2216
 excretion, rabbits, hens and cows: 2217

FIBRINOGEN

metabolism, transplanted mouse tumors: 974

FLOUR

occupational exposure, nasal cavity and sinus tumors, England (Northamptonshire): 1658

FLUORANTHENE

analysis, coffee substitutes: 1800

2-FLUORENAMINE

toxicity, insect (cockroach): 624

FLUORENE, 2-AMINO-

effect on liver microsomes, rat: 2240, 2241

FLUORENE, N-HYDROXY-2-AMINO-

mutagenesis (bacteria) and skin tumor-initiating effect (mouse): 1183

N-2-FLUORENYLACETAMIDE

bladder tumors, animal: 1171, 1850, 2253

brain tumors, effect of lead, rat: 1849

DNA or RNA binding, mechanism, rat liver: 1538, 2243, 2244, 2245

effect on

properties of oligonucleotides: 1929

Rous virus tumors, chick: 52

serum proteins, monkey: 62

tissue-specific inhibitor of DNA synthesis, rat liver: 1532

ultrastructure, pancreatic exocrine cells, rat: 64

WBC phagocytic activity, rat: 1180

liver tumors

mouse: 1843

rat: 3, 61, 416, 430, 671, 1202, 1560, 1842, 1844, 1845, 1846, 1847, 1848, 1852, 1939, 2247, 2248

mammary and ear duct tumors, rat: 417

metabolism, effect of germ-free status, rat: 434

- N-2-FLUORENYLACETAMIDE (contd.)
 protein binding, mechanism, rat liver: 2242
 synergism with polyoma virus, rat: 1202
 treated lung explant, s.c. tumors, mouse: 1462
- N-2-FLUORENYLACETAMIDE, N-ACETOXY-
 decomposition pathways: 2238
 effect on
 liver microsomes, rat or guinea pig: 2241
 RNA, bacteria: 2250
 mutagenesis (bacteria) and skin tumor-initiating effect (mouse): 1183
- N-2-FLUORENYLACETAMIDE, N-HYDROXY-
 binding
 DNA or RNA, rat liver: 2244, 2246
 protein, rat liver: 1540, 1852, 1853, 1854, 1855, 2242
 g.i. and bladder tumors, age factors, rat: 2249
 liver tumors
 rat: 1852, 1853, 1854, 1855, 2249
 susceptibility, carcinogen metabolism, species difference, rodent: 1550
 metabolism
 effect of sulfate ion, rat liver: 672
 germ-free rat: 433
 mutagenesis (bacteria) and skin tumor-initiating effect (mouse): 1183
- N-2-FLUORENYLACETAMIDE, N-HYDROXY-, ESTERS
 mutagenesis, bacteria: 2239
- N-2,7-FLUORENYLDIACETAMIDE
 liver tumors, effect of reserpine, sex factors, mouse: 1856
 premalignant liver lesions, hormone effects, rat: 424
- N,N'-2,7-FLUORENYLENEBISACETAMIDE
 effect on serum proteins, monkey: 62
 intestinal tumors, rat: 1857
 liver tumors, rat: 1468, 1508, 1857
- FLUORODEOXYURIDINE (See under Antitumor agents)
- FOOD ADDITIVES
 food coloring (Ponceau MX), liver toxicity, mouse: 609
 hexamethylenetetramine, toxicity, mouse or rat: 608
 liver or lung tumors and lymphoma, mouse: 1779
- FOOD PROCESSING METHODS
 drying, benzpyrene content of prunes: 2215
 fish smoking, benzpyrene content, gas combustion products: 2208
 wood smoke: 2209
 margarine or chocolate, carcinogen content, Germany: 604
 salt drying, benzpyrene content: 2210
 smoking of meat or fish, stomach cancer, Iceland: 2083
- FOODS (See also Dietary factors)
 aflatoxin content, products of African or French origin: 2296
 artificial sweeteners
 bladder cancer, U.S.: 2544
 cyclamates or cyclamate-saccharin mixture, bladder tumors, rat, review: 573
 effect on g.i. tract, mouse: 2315
 saccharin, bladder tumors, mouse: 1780
- FOODS (See also Dietary factors) (contd.)
 benzpyrene content, stomach cancer, Iceland: 2083
 carcinogens
 analysis, review: 161
 g.i. or liver tumors, animal or human, review: 1014
 coffee substitutes, carcinogen content: 1800
 contamination
 dimethylnitrosamine, South Africa (Transkei): 397
 mycotoxins, review: 366
 dimethylamine content, intragastric nitrosamine formation: 1529
Encephalartos hildebrandtii flour, kidney tumors, rat: 405
 fish, benzpyrene content processing methods: 2208, 2209
 heated fats and oils, s.c. or g.i. tumors, rat: 241
 margarine or chocolate, carcinogen content, processing methods, Germany: 604
 meats, aflatoxin content: 1104, 1105
 milk from benzpyrene-fed cows, benzpyrene uptake by calves: 2216
 nitrates, reduction to nitrosamine (gastric bacteria), human: 639
 nitrosamine content, review: 164
 prunes, benzpyrene content, drying methods: 2215
 refrigeration, aflatoxin production: 661
 salt, benzpyrene content, processing methods: 2210
 spinach, nitrosamine content, storage methods: 2278
 wheat flour, nitrosamine content, analytical method: 610
- FORMAMIDE, N-(4-[5-NITRO-2-FURYL]-2-THIAZOLYL)-
 bladder tumors
 mouse: 1908
 rat: 427, 1556
 kidney tumors, rat: 1556
- FORMIC ACID 2-(4-[5-NITRO-2-FURYL]-2-THIAZOLYL) HYDRAZIDE
 leukemia and solid tumors, mouse: 1907
- FREE RADICALS
 analysis, breast cancer, growth kinetics: 2612
- FUNGI
Candida albicans or Saccharomyces cerevisiae, polyoma virus propagation: 322
 carcinogen production, review: 162, 163
 effect of aflatoxins, review: 2121
 mycotoxins, foods, review: 366
 steroid-hydroxylating strains, aflatoxin metabolism: 662
- FUNGICIDES (See under Herbicides)
- GA VIRUS (See under Virus, herpes-type)
- GALLBLADDER NEOPLASMS
 epidemiology
 East Germany, cholelithiasis, sex difference: 130
 Finland, cholelithiasis: 899
 Germany (Göttingen-Weende): 1360
 Poland (Warsaw), cholecystitis: 1350

- LIUM
distribution, leukemic or nonleukemic AKR/J
mice: 1775
- GLIONEUROBLASTOMA
ultrastructure and catecholamine production,
child: 350
- GLIOSIDES
analysis, SV40- or spontaneously-transformed
tumor-inducing mouse cell lines: 515
- OLINE (See under Engine exhaust gases or
Petroleum and petroleum products)
- TROINTESTINAL CARCINOGENESIS
aflatoxin, hamster: 187
benzpyrene, rodent: 241, 1089, 1791
bracken extracts, rat: 68, 2314
colon/rectum cancer, single- or multiple-"hit"
theory: 2085, 2086
crude corn oil, mouse: 2328
dibutylnitrosamine, mouse or hamster: 248, 1537
dietary carcinogens, animal, review: 1014
diethylnitrosamine, mouse: 236, 1147, 1547
dimethylhydrazine, hamster or rat: 1905, 2273
N-disubstituted arylhydroxylamines, structure-
activity relationship, rat: 1562
ethyl-N'-nitro-N-nitrosoguanidine, rat or mouse:
1464
fluorenylacetylamide, effect of sunflower oil,
rat: 1842
fluorenylenebisacetamide, rat: 1857
formic acid 2-(4-[5-nitro-2-furyl]-2-thiazolyl)
hydrazide, mouse: 1907
heated edible fats and oils, rat: 241
hydroxyaminoquinoline oxide, rat: 428
hydroxyfluorenylacetylamide, age factors, rat:
2249
- intestinal tumors
aflatoxin analog (afutoxin), mouse: 1488
dimethylhydrazine, enzymes, rat: 1497
diphenylpropynyl-N-cyclohexylcarbamate, rat:
1563
2-(2-formylhydrazino)-4-(5-nitro-2-furyl)
thiazole and related agents, rat: 1548
methylnitrosourea, hamster: 1154
N-(4-[5-nitro-2-furyl]-2-thiazolyl)acetamide,
rat: 1510
nitroquinoline oxide, rat: 674
methylcholanthrene, guinea pig or mouse: 1899,
2191
methylnitrosoguanidine, rat or mouse: 1464,
1465, 1873, 1874, 1875
methylnitrosourea, transplacental, rat: 1876
5-nitrofur derivatives, rat: 417
nitroquinoline oxide, effect of alkylbenzene-
sulfonate vehicle, rat: 1476
nitrosamines, DNase and RNase, high- and low-
tumor sites, rat: 971
nitroso compounds, upper g.i. tract, tumor
pathology, rat: 638
nitrosopiperidine, mouse: 67
oral contraceptive, rat: 1830
pesticides, occupational, case and review:
1720
possible mechanism (nitrate reduction to
nitrosamine), human: 639
radiation, mouse: 167
sucrose, saccharin or sodium cyclamate,
negative results, mouse: 2315
- GASTROINTESTINAL CARCINOGENESIS (contd.)
s-triazine compounds, mouse or rat: 2272
- GASTROINTESTINAL NEOPLASMS
DNase and RNase activity, susceptible sites,
human: 1424
epidemiology
anesthesiologists, U.S. and Canada: 888
environmental temperature variations, U.S.:
1343
Oklahoma, ethnic groups, environmental
factors: 1648
sex ratio, England/Wales and western Europe:
1389
smoking, Poland: 542
trace metal content of drinking water,
Italy (Pesaro): 2072
familial, age-, sex- and site-related patterns:
1679
mother and children: 1669
upper, carcinoma, risk of second primary
tumor, New York: 1665
- GENETICS, ANIMAL
age-related spontaneous remission of Friend
viral leukemia, BDF₁ mice: 1630
autoimmunity, role of DNA and RNA, NZB/NZW
mouse: 444
cancer promotion, review: 1436
guinea pig strain susceptible to L2C/NB
leukemia, herpes-type virus isolation:
1328
hepatoma-susceptibility gene, liver and
hepatoma growth rate, mouse: 2618, 2619,
2620
high-fat diet-induced hepatoma, mouse: 250
high-spontaneous tumor hamster strains: 2097,
2642
host immunity and Moloney viral sarcoma
development, NZW x NZB hybrid mice: 2367
leukemia, role of hairless (hr) gene, mouse:
919
lung tumor-resistant mouse strain (C57BL),
methylcholanthrene effect on lung explants:
2188
mammary tumors
dogs, USSR (Moscow): 2098
pathology, NZB mice: 291
transplantability, virus-positive or -nega-
tive mice: 1997
mammary tumor virus
agent-free mice (R111B/DE), mammary and
other tumor incidence: 554
hereditary transmission and susceptibility,
mouse strains: 481
positive mouse strain, low spontaneous
mammary tumor incidence: 1253
Marek's disease virus antigen localization,
tumor and host cells, susceptible and
resistant chickens: 508
MH2 reticuloendothelioma virus resistance,
chickens: 1950
mouse strain
high susceptibility to very weak carcinogens:
1190
low or high low thyroidal ¹³¹I uptake: 2644
NZB mice
age-related lymphoid mast cell proliferation
and autoimmunity: 1706

GENETICS, ANIMAL (contd.)

- autoimmunity, virus-like particles: 871, 2332
- development of high- and low-cancer mouse strains, review: 1712
- effect of Rauscher leukemia virus on autoimmunity: 2347
- ovarian tumor-susceptible mouse strain, hormone metabolism and hair loss pattern: 2268
- possible latent virus and host immunity, high-plasma cell tumor mouse strain: 973
- preleukemic thrombocytopenia, AKR mouse strain: 154
- serum complement activity, NZB mice and hybrids: 972
- skin tumors
 - fish, species specificity, San Francisco Bay: 534
 - susceptibility or resistance, epidermal cell endoplasmic reticulum, mouse: 1422
- spontaneous mammary tumors, lung tumors and plasma cell lymphomas, PBA mouse strain: 2643
- strain differences
 - adenovirus-12 or SA-7 tumors, hamster: 2412
 - AKR leukemia virus susceptibility, mouse: 1983
 - benzpyrene hydroxylase activity, mouse liver: 2205
 - leukemia, mouse: 1479
 - blood mammary tumor virus activity, mouse: 1593
 - carbon tetrachloride hepatoma, rat: 420
 - dibutyl nitrosamine tumor spectrum, hamster: 1537
 - dimethylbenzanthracene sensitivity, mouse: 49, 1808
 - rat: 1073
 - FBJ sarcoma virus sensitivity, mouse: 814
 - Friend leukemia virus sensitivity, mouse: 1217, 1570, 2336, 2339, 2340, 2343
 - group-specific leukemia viral antibodies, high- or low-leukemia mouse strains: 2348
 - karyotype of Yoshida sarcoma, rat: 2665
 - leukemia virus infection, mouse: 1305
 - mammary tumor virus reactivity, mice: 1595, 1622
 - methylcholanthrene immunosuppression and skin carcinogenesis, mouse: 393
 - nickel-induced rhabdomyosarcoma, rat: 704
 - plastic implant tumors, mouse: 2300
 - radiation-induced ovarian tumors, mouse: 2178
 - Rauscher virus-induced lymphoma, mouse: 774
 - Rous sarcoma virus-induced tumors, rat: 1585, 2373
 - s.c. tumors induced by surgical adhesives, rabbit: 2306
 - spontaneous mammary and lung tumors, mouse: 983
 - surface antigens, leukemias of C57BL and other mouse strains: 2351
- testis tumors, Mexican axolotl (Ambystoma mexicanum): 2650

GENETICS, ANIMAL (contd.)

- thyroid cancer or parathyroid hyperplasia incidence, rat: 1433
- tumor growth and immunity, syngeneic or allogeneic host-mammary tumor systems, mouse: 2627

GENETICS, CELLULAR

- cell-associated factor required for infectious RSV(0) synthesis, chick embryo cells: 2385
- effect of chemical carcinogens, mechanism, review: 352
- gene-selection theory of carcinogenesis, review: 559
- polyoma virus DNA as biochemical tool for studies of genetic regulation, mammalian cells, review: 2144
- SV40- or polyoma-transformed cells, review: 580
- theory of malignant transformation, review: 13

GENETICS, HUMAN

- albinism, skin cancer, Nigeria: 1667
- bilateral carotid body chemodectomas, familial, case and review: 2653
- brain tumors, familial, Minnesota: 2580
- cancer promotion, review: 1436
- Chediak-Higashi syndrome, abnormal peripheral WBC cultures: 1407
- Christchurch chromosome, with/without mongolism, leukemia: 934, 1336
- chromosome abnormalities
 - cancer pts. and normal subjects: 956
 - cancer risk, review: 1010, 1733
- diabetes mellitus, cancer susceptibility: 541
- familial
 - age-, sex- and site-related patterns: 1679
 - arrhenoblastoma: 947
 - ataxia-telangiectasia, stomach cancer: 552
 - basal cell nevus syndrome, radiation-induced maxillary cancer: 2163
 - cancer: 1331
 - syndrome associated with childhood rhabdomyosarcoma: 1334
- esophagus cancer, siblings: 1669
- freckling patterns and neurofibromatosis: 1413
- immunity disorders with chronic leukemia: 959
- leukemia: 918, 943, 1333
- Japan: 2605
- multiple-case family (7 generations): 1678
- review: 586, 1437, 1447, 2152
- twins, review: 2136, 2152
- SV40-transformation susceptibility of skin fibroblasts: 1225
- lymphoma, Nebraska: 1333
- melanoma: 533, 2077
- identical twins: 1330
- review: 1718
- multicentric fibromatosis and desmoids: 543
- ovarian tumors, mother and daughters: 886
- sisters (adolescents): 2659
- pheochromocytoma, epinephrine-producing, with medullary carcinoma of thyroid: 948

NETICS, HUMAN (contd.)

- identical twin: 1408
- polyadenomatosis syndromes, review: 565
- soft tissue sarcomas with breast and other tumors: 914
- familial polyposis of colon
 - associated bone sarcomas, mother and child: 2655
 - Gardner's and Turcot's syndromes: 2654
 - soft tissue sarcomas: 958
- malignant transformation: 336, 1332, 2558, 2672
- sex cord tumor of ovary: 1403
- stomach cancer, child: 962
- haptoglobin and Gc group genotype, leukemia: 1397, 2595
- hepatoblastoma, siblings (infants): 131
- hereditary skin diseases, malignant transformation: 1742
- high-risk disorders, leukemia and lymphoma, review: 585, 2137
- HL-A transplantation gene, children with leukemia and their families: 547
- kidney tumors, siblings: 1409
- mongolism
 - acute leukemia, possible leukemia virus, review: 1026
 - congenital leukemia: 953
 - leukemia and other malformations, Massachusetts: 1335
- neuroblastoma: 2088
- non-leukemic tumors, children, twins, California: 1680
- serum LDH fractions, PTC tasting and blood groups, female genital cancer, Poland: 550, 551
- sickle cell trait genotype, Burkitt lymphoma, Uganda (Kampala): 2609
- skin cancer, review: 15
- susceptibility to chemical leukemogenesis: 1910, 1911
- Xg genotype, Ph¹-positive or -negative chronic myeloid leukemia: 1394, 1398

NETICS, MICROBIAL

- adenovirus-2 genome transcription, infected or transformed cells: 835
- Friend (strain F-S or F-B) leukemia virus, gene governing splenic focus formation: 2336
- mouse leukemia viruses, classification method: 2353
- mouse sarcoma virus genome, effect on carbohydrate uptake, transformed cells: 463
- polyoma virus, genome transcription pattern, mouse cells: 495
- SV40, lytically-infected or transformed mouse cells: 501
- monkey-mouse hybrid cell lines: 1278
- tumor viruses, review: 1729

NETICS, POPULATION

- cancer mortality, isolated community, Italy (Spoleto): 326
- myeloma globulin distribution, Japan and New York (white and Negro): 915
- nasopharynx cancer
 - Chinese and other Oriental populations, review: 568, 1719

GENETICS, POPULATION (contd.)

- Hong Kong, ethnic groups: 825
- South Vietnam: 330
- relative malignancy and occurrence of breast cancer, England and Africa (Nigeria and Uganda): 2562
- GENITAL NEOPLASMS
 - herpes simplex virus, review: 2147
 - venereal sarcomas, epidemiology, dogs, USSR (Moscow): 2098
- GENITAL NEOPLASMS, FEMALE
 - adenocanthoma of rectovaginal septum, transformed from endometriosis: 144
 - chromosomes: 342, 955
 - epidemiology
 - contraceptives, review (book): 557
 - ethnic groups, Oklahoma: 1353
 - Germany (Giessen), diabetes and hormonal factors: 1688
 - India (Bombay), Hindus and Parsis: 2066, 2067
 - New York (upstate): 2577
 - USSR (Kirovabad), ethnic groups: 2078
 - Fallopian tube tumors, epidemiology, New York (Long Island): 1358
 - genetic factors (serum LDH fractions, blood groups and PTC tasting), Poland: 550, 551
 - induction, ethylnitrosourea, pregnant rat: 723
 - multicentric tumors of cloacal origin, pathogenesis: 960
 - risk of second primary tumor, Connecticut: 909
- GENITAL NEOPLASMS, MALE
 - malignant or preinvasive, karyotype: 342
- GERM-FREE STATUS
 - age-related tracheobronchial gland development, mouse: 2102
 - effect on
 - autoimmunity and lymphoma, NZB mice: 1430
 - cycasin toxicity, rat, review: 995
 - dimethylbenzanthracene carcinogenesis, mouse: 611, 702, 703, 731
 - leukemia virus transmission, AKR mice: 755
 - mouse, review: 575
 - mammary tumor virus infection and transmission, mouse, review: 575
 - metabolism of fluorenylacetamide and derivative, rat: 433, 434
 - methylcholanthrene s.c. tumors, mouse: 611
 - radiation leukemogenesis, mouse: 589
 - Rous sarcoma virus oncogenesis, rat: 790
 - excretion of phenolic cocarcinogens, rat: 1489
 - mineral oil induction of plasma cell tumors, mouse: 1175
 - Rous sarcoma virus-induced leukemoid reaction, rat: 1301, 1953
 - spontaneous transformation, rat embryo cells: 1296
 - urethan-induced lung tumors, mouse: 411
- GLUCOSAMINES
 - membrane
 - normal mouse cells: 1287
 - virus-transformed mouse or hamster cells: 1287, 1324
- GLUCURONIDES
 - metabolism, effect of diethylnitrosamine, animal: 1927

GLUTATHIONE

biosynthesis, chemical carcinogenesis, review: 2122

GLYCERYL PALMITATE POLYMER

s.c. sarcoma, mechanism, rat: 1544

GLYCOPROTEINS

distribution, polyoma virus-induced hamster sarcoma: 862

GOLD THIOGLUCOSE

osteoma of skull, mouse: 718

GRISEOFULVIN

leukemia, human: 1201

GUANINE 3-N-OXIDE

s.c. tumors, rat: 1189

HEAD AND NECK NEOPLASMS

epidemiology

children, Sweden (Malmö): 2583

serum EB virus antibodies, international: 523

skin cancer, Sweden, sunlight: 2529

ethmoid and paranasal sinus tumors, occupational exposure to wood: 368

HEART NEOPLASMS

hemangioendothelial, occupational silicosis: 682

induction, dimethylurea + nitrite, rat: 1882

pericardial mesothelioma, asbestos induction, rat: 1101

HEMATOPOIESIS

effect of radiation and leukemia virus, mouse: 99

erythropoiesis

effect of virus-induced mouse leukemic cell cultures: 1640

Friend viral leukemia, mouse: 1568

erythropoietin-stimulating factor, effect of dimethylnitrosamine, monkey or dog: 1871

platelets, Rauscher virus leukemia, mouse: 261

preleukemic thrombocytopenia, AKR mice: 154

HEMOPEXIN

serum, effect of methylcholanthrene, rabbit: 1903

HEPARIN

effect on

lung metastases, syngeneic mouse tumors: 1469

transplanted tumors, mouse: 2302

HEPATECTOMY (See under Liver)

HERBICIDES (See also Pesticides)

effect on glycolysis, rat liver: 2263

fungicides, liver and other tumors, mouse: 31

occupational exposure, stomach cancer, case and review: 1720

skin and g.i. tumors, mouse or rat: 2272

zinc-dithiocarbamic acid type, lung tumors, mouse: 1778

HEXAMETHYL-DEWAR-BENZENE (See Bicyclo(2.2.0)hexa-2,5-diene, hexamethyl-)

HEXAMETHYLENETETRAMINE (food additive)

toxicity, mouse and rat: 608

HISTAMINE

antagonists and inhibitors, effect on protein synthesis, rat tumors: 1243

HISTONES

content, methylnitrosourea- or trimethyl-benzanthracene-induced brain tumors, rat: 632

synthesis, polyoma- or SV40-infected cells: 2018

HODGKIN'S DISEASE (See under Lymphoma, malignant, human)

HORMONES (general and unspecified; see also Endocrine ablation and specific hormones) carcinogenesis, role of pituitary-adrenal system, review: 2120

dependence, androgen + estrogen-induced uterine leiomyosarcoma, hamster: 1833

effect on

dimethylbenzanthracene mammary tumors, rat: 219, 2228

DNA, virus-induced hyperplastic alveolar mammary nodules, mouse: 292

fluorenyldiacetamide liver tumors, rat: 424

hydrazine lung carcinogenesis, mouse: 1498

methylcholanthrene-induced prostate tumors, rat: 1052

growth-stimulating or -retarding, production and effects on normal and malignant cells, review: 563, 564

insect, juvenile hormone-like substances, melanotic tumor induction, *Drosophila*: 1194

metabolism

breast cancer, review: 583, 1724, 1725

endometrial cancer: 1136, 1357, 1431

female genital cancer, Germany (Giessen or Munich) and Japan (Osaka): 1688, 1690

ovarian tumor-susceptible mouse strain: 2268

pre- and postmenopausal breast cancer

epidemiology, Germany (Berlin): 2080

pituitary graft, effect on hyperplastic alveolar mammary nodule, mouse: 710, 819

prolactin

effect on transplantable mammary tumors, mouse: 2267

metabolism, estrone-induced or spontaneous pituitary tumors, rat: 728

spontaneous mammary tumors, rat: 728

radioimmunoassay, normal pituitary or prolactin-producing pituitary tumor, rat: 727

secretion, estradiol-induced pituitary adenoma, rat: 1501

sensitivity, SV40-induced hamster prostate tumors: 506

HORMONES, CONTRACEPTIVE

breast cancer, human: 1125

cervix cancer: 1127

Czechoslovakia: 911

mouse: 715, 1554

New York City: 1387

effect on

chemical mammary carcinogenesis, rat: 56

mammary tumor incidence, mouse: 1503

nucleic acids and protein, human cervix: 1425

fibroadenoma of breast, human: 1126, 1806

mammary and genital cancer, animal and human, review: 2

- RMONES, CONTRACEPTIVE (contd.)
 multiple tumor types, rat: 1830
 pregestational, effect on cervix cancer
 induction, mouse: 1128
- RMONES, GONADOTROPIC
 feedback mechanism, normal pregnancy and
 trophoblastic tumors: 967
 ovarian response, effect of dimethylbenzanthra-
 cene, mouse or rat: 216
- RMONE, SOMATOTROPIC
 effect on
 methylcholanthrene skin tumors, mouse: 1055
 transplantable mammary tumors, mouse: 2267
 secretion, estradiol-induced pituitary tumor,
 rat: 1501
- RMONES, STEROID
 biosynthesis, spontaneous interstitial cell
 tumor of testis, mouse: 1506
 effect on protein synthesis, human WBC: 1192
 endocrine and other tumors, animal, review:
 999
 placental, feedback mechanism, normal pregnancy
 and trophoblastic tumors: 967
- RMONES, THYROID
 effect on methylcholanthrene sarcoma, rat:
 1502
- ANTIOIN COMPOUNDS
 anticonvulsants, lymphoma, human: 1909, 1910
- ANTIOIN, DIPHENYL-
 effect on bladder, rat: 1912
- ORAZINE, 1,1-DIMETHYL-
 alkylating action, rat tumor: 1146
- ORAZINE, 1,2-DIMETHYL-
 intestinal or duodenal tumors, rat: 1497, 2273
 liver and g.i. tumors, hamster: 1905
- ORAZINE, N-METHYL-, DERIVATIVES
 metabolism, rat liver microsomes: 1496
- ORAZINE COMPOUNDS
 leukemia and lung or skin tumors, structure-
 activity relationship, mouse: 58, 252
- ORAZINE SULFATE
 liver tumors (mouse) and liver toxicity
 (hamster): 1500
 lung tumors, mouse: 1498, 1499
- YDRAZINOTHIAZOLE COMPOUNDS
 structure-activity relationship, rat: 1906
- ROCARBONS
 biosynthesis, yeast culture grown on benz-
 pyrene-containing diesel oil: 2207
 carcinogenic or non-carcinogenic, binding to
 DNA and RNA, normal cells: 232
 halogenated, anesthetics, effect on
 diethylnitrosamine carcinogenesis, mouse: 236
 mechanism of action, review: 2123
- ROCARBONS, POLYCYCLIC AROMATIC
 analysis
 air or atmospheric dust, methods: 603, 1786
 water supply, method: 1785
 breakdown rate of carcinogenic and non-
 carcinogenic compounds, mouse embryo cells:
 2219
 DNA photosensitization: 2203
 effect on benzpyrene metabolism, rat liver
 microsomes: 205
 mechanism of action, review: 165
 theoretical model: 1084
- HYDROCARBONS, POLYCYCLIC AROMATIC (contd.)
 metabolism, effect of benzpyrene, rat liver:
 640
 structure-activity relationships: 599, 1783
- HYDROCORTISONE
 effect on skin carcinogenesis, mouse: 1486
 metabolism, breast cancer: 1412
- HYDROCORTISONE ACETATE
 effect on transplanted tumor, sex difference,
 mouse: 1507
- HYDROXYLAMINE
 effect on DNA, bacteriophage: 1168
 mutagenesis, bacteria: 2252
- HYDROXYLAMINE, 1- OR 2-NAPHTHYL-
 s.c. tumors, mouse: 69
- HYDROXYLAMINE COMPOUNDS
 N-acylaryl derivatives, structure-carcinogenic
 activity relationship, mammary and other
 tumors, rat: 2251
 N-disubstituted arylhydroxylamines, g.i.
 tumors, structure-activity relationship,
 rat: 1562
- HYDROXYUREA (See under Antitumor agents)
- HYPOPHYSECTOMY (See under Endocrine ablation)
- HYPOTHALAMUS
 estrogen implant, stimulation of DMBA mammary
 tumor, rat: 1821
 injury, effect on induced mammary tumors, rat:
 54
- IMMUNE SERUM
 antilymphocyte serum
 effect on
 dimethylbenzanthracene tumors, mouse or
 hamster: 697, 703
 herpesvirus infection, mouse: 875
 methylcholanthrene tumors, mouse: 391
 polyoma virus-induced runting and tumor,
 hamster: 2058
 syngeneic tumor-host system, mouse: 146
 transplantability of bovine lymphosarcoma,
 calf: 469
 transplantable tumors, mouse: 623
 host immunity induction, polyoma virus-
 infected mouse: 864
 antithymocyte serum
 stimulation of plasma cell tumors, mouse:
 1197
 effect on
 Harvey sarcoma virus carcinogenesis, mouse
 or rat: 109
 methylcholanthrene-induced tumors, mouse:
 1472, 1512, 2183
 Moloney viral sarcoma, mouse: 1635
 Rauscher viral leukemia, mouse: 1580
 transplanted tumors, mouse: 1472
 urethan lung carcinogenesis, mouse: 1526
 viral lymphoma, mouse: 102
 Friend leukemia virus antiserum, production,
 mouse, rat or rabbit: 1976
 lung injury, effect on nitroquinoline oxide
 lung carcinogenesis, mouse: 1475
 pooled human immune globulin, effect on EB
 virus-infected human leukemia or lymphoma
 cells: 1615

IMMUNITY

precipitation reaction between tobacco extracts and human sera: 1769

IMMUNITY, CELLULAR

adenovirus, infected, transformed or tumor cells: 482, 1266, 2003, 2401, 2402, 2407, 2408, 2411, 2415, 2511

adenovirus-SV40 hybrid-transformed cells: 2419, 2421, 2423

antibodies to HeLa cell antigens, human tumors: 751

avian leukosis-sarcoma virus complex: 284, 466, 1244, 1313, 2374, 2380, 2384

carcinogen-induced tumors, animal: 11, 203, 395, 655, 656, 657, 658, 1442, 1541, 1578, 2141, 2185, 2229

Epstein-Barr virus-containing cells: 300, 827, 828, 829, 1617, 1633, 2039

feline leukemia virus, lymphomas from cats and other mammals: 447

hamster tumor induced by human leukemic WBC culture: 151

herpesvirus-infected cells: 824, 1325

lymphocyte transformation by tumor extracts, breast cancer: 546

Marek's disease virus, infected or tumor cells: 508, 2483, 2484, 2485

mouse mammary tumor virus: 285, 288, 1595, 1596, 2399

papilloma virus, transformed or tumor cells: 308, 489, 1270

polyoma virus, infected, transformed or tumor cells: 312, 492, 496, 580, 1273, 1324, 1325, 2011, 2432, 2457, 2458

rodent leukemia-sarcoma virus complex: 108, 271, 445, 446, 762, 1578, 1582, 1628, 1636, 1980, 2335, 2341, 2351, 2354, 2505

Shope fibroma virus-infected rabbit cells: 2474

spontaneous mammary tumor, virus-free mouse strain: 2053

structure and antigenicity of tumor cell plasma membrane lipids: 1429

SV40, infected, transformed or tumor cells: 119, 313, 580, 848, 849, 850, 851, 874, 1277, 1322, 1323, 1324, 1606, 1631, 1641, 2021, 2027, 2062, 2432, 2433, 2448, 2449, 2450, 2507, 2509

T5 mouse tumor: 149

tumor mitochondria-specific antigen(s), exptl. tumors: 788, 1435

virus-induced tumors, review: 11, 354, 1009, 1442, 1731, 2143

virus-specific antigens, carcinogen- or radiation induced mouse lymphoma: 1203

IMMUNITY DISORDERS

autoimmunity

effect of polyoma or Rauscher viruses, NZB mice: 2048, 2063, 2347

lymphoid mast cell proliferation, age factors, NZB mice: 1706

malignant transformation, germ-free NZB mice: 1430

role of DNA and RNA, NZB/NZW mouse: 444

virus infection, cancer pathogenesis, review: 1025

IMMUNITY DISORDERS (contd.)

virus-like particles, NZB mice: 871, 2332
chimerism, induction, methylcholanthrene + irradiation, rat: 1046

CNS disease induced by syngeneic transplantable leukemia, age factors, mouse: 2331

congenital hypogammaglobulinemia with Hodgkin's disease, case (child) and review: 2107

dermatomyositis, association with cancer, cases and review: 1704

graft-versus-host reaction, lymphoma incidence, mouse: 1199

immunoglobulin deficiency with leukemia, familial: 959

leprosy, cancer risk, U.S.: 880

lupus vulgaris, malignant transformation: 595

lymphoma risk, review: 585

rheumatic type, leukemia incidence, Western Australia: 2625

rheumatoid arthritis, lymph node follicular hyperplasia: 339

runting

effect of Metopirone, tumor incidence, rat: 556

polyoma virus-induced, effect of anti-lymphocyte serum, hamster: 2058

tumor induction, mouse: 1200

scleroderma, malignant transformation, case (bronchial cancer) and review: 2153

systemic lupus erythematosus, malignant transformation (leukemia or lymphoma): 337, 2639

IMMUNITY, HOST

adenoviruses, tumor-bearing hamster or infected monkey: 1603, 2402, 2406, 2413, 2416

age changes, high-plasma cell tumor mouse strain: 973

avian leukosis-sarcoma virus complex, infected or tumor-bearing birds or mammals: 319, 797, 800, 1244, 1586, 2373, 2382

carcinogen-induced tumors or effect of carcinogens, rodent: 42, 43, 51, 59, 367, 389, 392, 394, 399, 415, 614, 677, 1063, 1209, 1541, 1809, 2196

effect of thymectomy, thymoma-bearing mouse: 431, 1198

exptl. or human tumors, review: 16, 566, 991, 1436, 1437, 1446, 2141

herpes-type viruses, frog, chicken or mammal: 1258, 2484, 2489, 2493

human

adeno-associated virus antibodies, cancer pts.: 2589

adenovirus antibodies, cancer pts.: 825, 834, 2588

Epstein-Barr virus

cancer pts.: 87, 509, 523, 825, 826, 2148, 2481

detection methods: 87

normal subjects: 296, 509, 1616

hepatitis-associated (Australia) antigen, leukemia or Hodgkin's disease: 2591

herpesvirus antibodies, cervix cancer: 2576

MUNITY, HOST (contd.)

- HL-A transplantation gene, children with leukemia and their relatives: 547
- leukemia- or sarcoma-specific antibodies, pts. and their relatives: 815, 1591, 1969
- loss of serum opsonin activity, cancer pts.: 1416
- lung cancer, air pollution, England and Wales: 1660
- mixed-cell agglutination reaction and ABH antigens: 2626
- neonatal vaccination with SV40-containing polio vaccine, cancer incidence: 316
- normal pregnancy or trophoblastic tumors: 967
- tumor growth rate: 945

- induction of tumor-specific transplantation immunity, animal: 789, 845

L-1210 mouse leukemia: 1993

- leukemia-sarcoma virus complex, rodent: 109, 262, 263, 279, 437, 439, 441, 763, 764, 768, 770, 773, 808, 814, 1227, 1570, 1574, 1575, 1576, 1629, 1972, 1982, 1987, 2064, 2343, 2344, 2345, 2348, 2354, 2367, 2633

- mouse mammary tumor virus: 288, 2053, 2396

- polyoma virus, infected or tumor-bearing animal: 855, 856, 864, 865, 2013, 2457

- radiation effects, mathematical model, mouse tumor: 940

- relationship to tumor growth rate, exptl. tumors: 945, 2627

- spontaneous or induced tumors, immunogenicity, mouse: 1248

- SV40, infected or tumor-bearing animal: 315, 850, 1603, 2023, 2428, 2431, 2440

MUNITY, VIRAL

- adenovirus-12, group-specific antigen, properties: 838

- avian leukosis-sarcoma virus complex, properties: 777, 778

- Epstein-Barr virus, capsid antigens, comparison with herpes simplex: 2480

- mouse leukemia-sarcoma complex, properties: 271, 435, 762

IMMUNOSUPPRESSION

- adenovirus-16, Sendai virus-infected hamster: 2418

- azathioprine, induction of cervical dysplasia, human: 705

- cyclophosphamide, Moloney virus-induced sarcoma, mouse: 808, 1589

- dimethylbenzanthracene, newborn or adult mouse: 614

- Friend-associated virus (Rowson-Parr virus), mouse: 1216

- Friend leukemia virus, normal or tumor-bearing mouse: 766, 1972, 2064, 2338

- kidney transplantation, induction of RES tumors: 2087

- malaria, effect on Harvey viral sarcoma, mouse: 1960

- methylcholanthrene, mouse: 393, 1511

- Metopirone, chronic runt disease, rat: 556

- Moloney sarcoma virus, mouse: 2370

- Rauscher leukemia virus, mouse: 262, 1219, 1318, 2347

IMMUNOSUPPRESSION (contd.)

- spleen cells, Moloney sarcoma virus-induced mouse tumors: 1589

- SV40, hamster: 767, 2418

- thymectomy, effect on urethan lung carcinogenesis, mouse: 1526

- urethan, mouse: 1527

IMMUNOSUPPRESSIVE AGENTS

- effect on viral lymphoma, mouse: 102

INDENE, 1(4-DIMETHYLAMINO)BENZAL)-

- mammary and s.c. tumors, rat: 53

INJURIES (See also Scar tissue and Stress)

- birth, brain tumors, adults and children, Minnesota: 2580

- bone, sarcoma, Paget's disease: 1404

brain

- implanted carcinogen, obesity induction, mouse: 620

- malignant transformation, child: 1738

- burns, malignant transformation, skin cancer: 1458, 1740, 2158, 2162

- caustic esophageal stenosis, malignant transformation: 360, 1457, 1741, 2159

- cervix cancer, human: 1737

- dental prosthesis, hard palate tumors: 1739

- electricity, effect on induced or transplantable tumors, rat: 1750, 2181

- lung, antiserum-induced, effect on nitroquinoline oxide lung tumors, mouse: 1475

- mechanical, skin cancer: 2153, 2657

- phagedenic ulcer of leg, malignant transformation, Senegal: 24

- pre-malignant tumors of lip: 394

- radiation dermatitis, skin cancer: 1740, 1743

- skin, intramitochondrial dense body, mouse: 2184

INKS (See under Dyes and stains)

INSECTICIDES (See also Pesticides)

- DDT, toxicity, lung, mouse: 701

- mutagenic, screening method, mouse: 1555

INSECTS

cockroach

- benzpyrene-induced abnormal cellular responses (non-hemocytic cells of midgut and hindgut): 625

- carcinogen toxicity: 624

- densonucleose virus (DNA-containing), transformation, mouse cells: 516

Drosophila

- carcinogen-induced mutations: 1760

- high- or low-tumor strains, effect of phthalate compounds and other agents: 626

- melanotic tumor strain, tumor induction, juvenile hormone-like substances: 1194

- mutagenesis, dimethylbenzanthracene: 382

- SV40 or Rous sarcoma virus: 517

- urethan metabolites: 2289

- SV40 or Rous sarcoma virus tumors: 517

mosquito (Aedes)

- vector transmission of hamster tumor (TM lymphoma): 555

INTERFERON

antagonists

- isolation, human soft tissue sarcomas: 467

- Moloney sarcoma virus-induced T-MSV

- hamster tumor: 462

INTERFERON (contd.)

effect on

Friend virus leukemogenesis, mouse: 2346
leukemia incidence and radiation-induced
kidney disease, RF/Un mice: 1040
Moloney sarcoma virus-transformed mouse
cells: 1955

spontaneous leukemia, AKR mouse: 443

loss of responsiveness, mechanism, Moloney
sarcoma virus-infected mouse embryo cells:
805

INTERFERON INDUCERS

effect on

mouse sarcoma or leukemia viruses in vitro:
843

viral carcinogenesis, review: 2140

INTERFERON INDUCTION (See also Statolon)

attempted, mouse mammary tumor virus: 823

effect on

Friend leukemia virus infection, mouse:
1321

Moloney sarcoma or Friend leukemia virus
in vitro: 1235

synthetic copolymer, effect on viral leukemia,
mouse: 97

INTESTINAL NEOPLASMS

induction, hydroxyaminoquinoline oxide, rat:
428

INTESTINE, LARGE, NEOPLASMS

epidemiology, dietary protein, international:
1432

induction

dimethylhydrazine, rat: 2273

fluorenylenebisacetamide, rat: 1857

malignant or preinvasive, karyotype: 342

risk of multiple primary tumors: 1359

second primary tumor, risk, breast or
female genital cancer, Connecticut: 909

INTESTINE, SMALL, NEOPLASMS

epidemiology

Japan: 2554

Michigan (Detroit): 2553

ileum or cecum, bracken extract-induced, rat:
2314

induction

dimethylhydrazine, rat: 2273

fluorenylenebisacetamide, rat: 1857

malignant transformation of regional enteritis:
1410

IODINE, RADIOACTIVE (See under Radioactive

isotopes and elements)

IODINE DEFICIENCY

with or without ¹³¹I, thyroid tumors, rat:
2265, 2266, 2629

IODODEOXYURIDINE (See under Antitumor agents)

IRON

plasma, normal and tumor-bearing rat: 2652

IRON DEXTRAN

s.c. sarcoma, rat: 233

ISOENZYMES

glutamic-oxaloacetic transaminase

serum, human cancer: 344

lactate dehydrogenase

distribution, female genital cancer, Poland:
550, 551

effect of dimethylbenzanthracene, human
fibroblasts: 211

ISONICOTINIC ACID HYDRAZIDE

lung tumors

animal and human: 1159, 1441

mouse: 252, 1499

toxicity, hamster: 421

treated lung explant, s.c. tumors, mouse: 1462

ISOPROTERENOL

effect on DNA, rat salivary gland: 1930

ISOTHIOCYANATE, ALLYL-

epidermal hyperplasia, mouse skin: 1188

ISOTHIOCYANATE, α -NAPHTHYL-

effect on liver RNA, rat: 201

liver tumors, specific biochemical abnormalities
rat: 1173

JOINT NEOPLASMS

chondrosarcoma, Maffucci's syndrome: 965

KIDNEY

calf, cell line (CK-66), virus-like particles:
752

dimethylbenzanthracene binding, DNA, rat:
1801

embryonic, effect of transplacental carcinogens,
mouse: 2128, 2224

β -naphthylamine binding, DNA, RNA and protein,
mouse: 1851

nitrosamine breakdown in vitro, rat: 644

radiation-induced glomerulosclerosis,
relationship to leukemia, RF/Un mouse
strain: 1040

toxicity

dimethylnitrosamine, monkey or dog: 1871

lead acetate, hamster: 720

KIDNEY CARCINOGENESIS

aflatoxin

hamster: 187

rat: 362, 363

cycasin, rat: 258, 719, 1774

diethylnitrosamine, mouse leukemia virus
antigen content: 408

diethylstilbestrol, hamster: 72

dimethylbenzanthracene, rat: 1820

dimethylnitrosamine, rat: 243, 721, 725,
1145, 2280

dimethylurea + nitrite, rat: 1882

Encephalartos hildebrandtii flour, rat: 405

fluorobiphenylacetamide, rat: 1858

2-(2-formylhydrazino)-4-(5-nitro-2-furyl)

thiazole and related compounds, rat: 1548

lead acetate

frog: 2309

mouse: 720

lead nitrate, frog: 2309

methylnitrosourea, rat: 37, 1876

5-nitrofur derivatives, rat: 417

N-(4-[5-nitro-2-furyl]-2-thiazolyl)acetamide,
rat: 1510

N-(4-[5-nitro-2-furyl]-2-thiazolyl)formamide,
rat: 1556

phenacetin abuse, human: 1123, 2545

polyoma virus + fluorenylacetamide, synergism,
rat: 1202

tobacco, review: 1715

transplacental, mouse or rat: 714, 1876

- KIDNEY CARCINOGENESIS (contd.)
triploid or normal frog larvae: 2045
- KIDNEY NEOPLASMS
epidemiology
children, Brazil (São Paulo): 1681
phenacetin abuse, Sweden: 1123, 2545
review: 581
smoking, U.S.: 1337
- Lucké adenocarcinoma (frog)
cytoplasmic virus particles: 2495
epidemiology, Minnesota, North Dakota and Louisiana: 2494
plasmacytoma in recipient, virus-like particles: 2496
temperature effect on virus development: 2492
viral latent period: 2490
nuclear RNA fractionation: 950
polyoma virus-induced sarcoma, rat: 866
spontaneous, virus-like particles, BALB/cf/Cd mice: 307
transitional cell carcinoma, exfoliative cytological diagnosis, standards: 2660
- Wilms' tumor (child)
associated pseudohermaphroditism, hypertension and renal degeneration, cases: 2106
transformed culture, papovavirus-like particles: 90
or metanephric hamartoma, siblings: 1409
- KUNITZ' PLASMIN INHIBITOR
effect on transplanted tumors, mouse: 2302
- LACTATION
breast cancer epidemiology
Greece (Athens): 2079
international: 2565
Japan (Tokyo): 2566
Massachusetts (Boston): 1356
effect on dimethylbenzanthracene mammary carcinogenesis, rat: 57
mammary tumor virus
isolation from milk, mouse: 473, 474, 475, 477, 478
replication sequence, mouse: 477
transmission, high-tumor strain (IBA/Gf) to low-tumor strain (X/Gf) mice: 1642
- ACTIONES
mechanism of action, animal, review: 1001
- ARYNX
pathology, smokers: 178
- ARYNX NEOPLASMS
cell growth kinetics, measurement method: 2614
epidemiology
blood groups, East Germany: 1670
Poland (Cracow): 528
smoking and occupation, Czechoslovakia: 881
Ukrainian SSR (Kirovograd), occupation and geographical variations: 2534
sex hormone metabolism, women: 1835
- EAD
analysis, cigarette tobacco and smoke: 686
- EAD ACETATE
endocrine tumors, rat: 1131
- LEAD ACETATE (contd.)
kidney tumors (mouse) and toxicity (hamster): 720
lung and kidney tumors, nucleolar abnormalities, frog: 2309
- LEAD NITRATE
lung and kidney tumors, nucleolar abnormalities, frog: 2309
- LEAD SUBACETATE
effect on fluorenylacetamide brain tumors, rat: 1849
- LEATHER
dust, occupational exposure (shoe manufacturing), nasal cavity and sinus tumors, England (Northamptonshire): 1658
- LECITHIN
brain tumors, mouse: 1493
- LEPROSY
cancer epidemiology, U.S.: 880
- LEUKEMIA, EXPERIMENTAL (See also Virus, leukemia/lymphoma)
avian myeloblastosis virus-induced viral RNA and cellular DNA, chicken: 2378
- C-1498 (mouse)
liver or spleen RNase and RNase inhibitor: 343
- C58BL mouse strain
surface antigens: 2351
- canine
cellular transmission: 2112
tumor pathology, mouse: 2046
- cell-transmitted
properties, mouse: 1228
virus particles, guinea pig: 1644
- CFW_w cell-transmitted (mouse)
leukemia virus particles: 756
- dimethylbenzanthracene-induced (EL4)
cell surface antigens, mouse: 1578
- E(AKR) leukemia (Gross leukemia virus-induced)
effect of anticoagulants, mouse: 2302
- erythroleukemia or erythremic myelosis
feline leukemia virus particles, cat: 761
- genetic susceptibility, role of hairless (hr) locus, mouse: 919
- human-type acute lymphoblastic, Opler virus-induced, guinea pig: 1226
- I_b (mouse)
immunization, CNS disease, age factors, mouse: 2331
- incidence, effect of radiation and interferon, RF/Un mouse strain: 1040
- L-1210 (mouse)
primary antibody response: 1993
- L2C (guinea pig)
cellular transmission, Strain 2 or hybrid guinea pig: 2634
chromosomes, antigenicity and role of virus: 2633
- L2C/NB (guinea pig)
herpes-type virus, susceptible guinea pig strain: 1328
- L5178Y (mouse)
cells, effect of arboviruses: 2049
- mineral oil + androgen-induced
myelomonocytic, chromosomes and muramidase content, mouse: 406

LEUKEMIA, EXPERIMENTAL (contd.)

- Moloney (viral)
 - effect of rat virus (RV-13 or 9HV-B), rat: 101
 - mouse, virus-induced, cell cultures, erythropoietic activity: 1640
 - Mycoplasma neurolyticum*-infected mice: 1232
 - P-1081 radiation-induced
 - growth-enhancing substance, mouse embryo cells: 975
 - radiation-induced
 - karyotype, AKR/T1ALD mouse: 361
 - Rauscher leukemia virus-induced
 - pathology, mouse: 771, 775
 - rat: 771, 772
 - SN-36 (mouse)
 - liver or spleen RNase and RNase inhibitor: 343
 - spontaneous
 - effect of interferon, AKR mouse: 443
 - transplacental methylnitrosourea, AKR mice: 2282
 - Fischer rat: 1229
 - karyotype, AKR/T1ALD mouse: 361
 - preleukemic thrombocytopenia, AKR mice: 154
 - thymic lymphocytic
 - virus particles, cat: 104
 - tissue distribution of gallium, AKR/J mice: 1775
 - viral etiology, review: 578
 - virus-containing chloroma (mouse)
 - properties: 264
- LEUKEMIA, HUMAN
- acute erythroleukemia
 - G-trisomy in leukemic cells: 2637
 - acute lymphoblastic
 - cell size variations and clonal evolution: 540
 - acute myeloid
 - cell size variations and clonal evolution: 540
 - with infectious mononucleosis, serum Epstein-Barr virus antibodies, case: 2482
 - XY/X0 mosaicism with group G deletion: 954
 - malignant transformation of systemic lupus erythematosus: 337
 - aging, review: 1013
 - associated with solid tumors, pathogenesis, cases and review: 1727
 - cell growth kinetics: 921
 - cell lines
 - hamster tumors: 150, 151
 - herpes-type virus: 84, 86, 298, 299, 829, 1614, 1615, 2631
 - properties: 2099, 2114, 2631, 2663
 - cell-free extract
 - transformed embryonic cell lines, chromosome markers and herpes-type virus: 88
 - cells
 - effect on amphibia and reptiles: 2383
 - karyotype, in vitro and in hamster: 320
 - child
 - HL-A transplantation gene, pts. and their families: 547
 - infectious mononucleosis, Epstein-Barr antibodies: 89

LEUKEMIA, HUMAN (contd.)

- chromosomal DNA content: 982
- chromosomes, review: 1010, 2152
- chronic granulocytic
 - griseofulvin-induced, chromosomes: 1201
 - irradiated Hodgkin's disease, chromosomes: 1460
 - Ph¹ chromosome: 156, 157, 2635
 - Xg genotype and Ph¹ chromosome: 1394, 1398
- chronic lymphocytic
 - associated immunity disorders, familial: 959
 - Kaposi's disease of skin, pathogenesis: 1707
 - Ch¹ chromosomal anomaly, familial: 934
- chromosomes: 2636
- immunity, review: 16
- incidence of second primary tumor: 882
- lymphocyte transformation capacity: 1423
- progressive multifocal leukoencephalopathy, polyoma virus-like particles: 2471
- culture fluid-transformed embryonic cell line (THE-3)
- cross-reactivity with Burkitt lymphoma sera: 302
- cytomegalovirus infection complicating chemotherapy: 1612
- epidemiology
 - anesthesiologists, U.S. and Canada: 888
 - Australia, rheumatic disorders: 2625
 - California (Los Angeles)
 - children: 1345
 - clustering: 1700
 - Canada (Saskatchewan), children: 1377
 - clustering, adults or children: 126, 917, 1675, 1676, 1677, 1700, 2093, 2094, 2095
 - Connecticut, clustering: 2094
 - dermatoglyphic defects, children: 145, 916
 - Europe, environmental factors, review: 2135
 - France, reproductive histories: 2594
 - genetic factors: 918
 - Georgia (Atlanta), ethnic groups: 2593
 - haptoglobin and Gc group genotype: 2595
 - hepatitis-associated (Australia) antigen distribution: 2591
 - high-risk associated disorders, review: 585, 1733, 2137
 - Hungary, children: 1348
 - Japan: 2596
 - age-related incidence changes: 1674
 - children: 126, 1673, 1675, 1676
 - clustering: 126, 1675, 1676, 2095
 - correlation with other tumors: 2601
 - familial: 2605
 - geographical variations: 2597, 2598, 2599, 2600
 - Hiroshima/Nagasaki: 592, 1672, 2602, 2603
 - occupational or therapeutic radiation exposure: 561, 2166, 2167, 2168, 2604
 - Maryland (Baltimore), children, seasonal onset: 2590
 - New England, clustering: 1677
 - New York, occupational asbestos exposure: 1763
 - perinatal and congenital, children, twins, review: 2136

LEUKEMIA, HUMAN (contd.)

Poland

dermatoglyphic patterns: 916, 1391
Gc blood group distribution: 1397
seasonal solar activity, Cracow: 1392
review: 586, 1016

U.S.

leprosy: 880
metropolitan areas, ethnic groups (Jews, Russians and Poles): 2592
Wisconsin (Green Bay), children, congenital defects, clustering: 2093

familial: 943

cases and review: 1447
Japan: 2605
multiple-case family (7 generations): 1678
Nebraska: 1333
SV40-transformation susceptibility of skin fibroblasts: 1225

lymphocyte blastoid transformation, review: 560

mongolism

chromosome abnormalities, child: 953, 1406
Christchurch (Gp⁻) chromosome, familial: 1336

frequency of associated malformations, children, Massachusetts: 1335

possible leukemia virus, review: 1026

multiple-case house, Georgia: 917

pathogenesis

DNA, RNA and enzyme cytochemistry, review: 1438

role of thymus, review: 991

properties of WBC RNA: 1968, 1970

screening for virus particles: 83

serum antibodies

herpes-type virus, detection methods: 87
to leukemic antigens, pts. and their relatives: 1969

SV40, children: 1605

transmission

baboons or macaques, virus-like particles: 2503

mice: 1228, 2046, 2502

virus etiology, review: 578, 2146

LEUKEMIA VIRUS (See Virus, leukemia/lymphoma)

LEUKEMOGENESIS, EXPERIMENTAL (See also Radiation leukemia/lymphoma)

3-acetaminophenanthrene, rat: 246

allogeneic, BALB mice infected with AKR

leukemia virus: 1572

benzidine, rat: 2233

benzidinedicarboxylic acid, rat: 1923

benzpyrene, strain differences, mouse: 1479

chicken erythroblastosis virus, rat: 754

compounds related to urethan, mouse: 58

cycasin, mouse: 2303

detergent additives (acenaphthenes), mouse or rat: 1772

dimethylbenzanthracene

hamster: 74

mouse: 76, 210, 220, 377, 731, 1808, 1809, 1810, 1811, 2389

rat: 44, 212, 374, 729

dimethylnitrosamine

leukemia virus activation, mouse: 408

LEUKEMOGENESIS, EXPERIMENTAL (contd.)

thymic lymphoma, mouse: 402

diphenylpropynyl-N-cyclohexylcarbamate, mouse, rat or Mongolian gerbil: 1563

DNA from human or hamster (papovavirus-induced) tumors, hamster lymphoma: 488

ethylnitrosourea, mouse: 2282

food additives, lymphoma, mouse: 1779

formic acid 2-(4-[5-nitro-2-furyl]-2-thiazolyl)hydrazide, mouse: 1907

hexamethylbicyclo(2.2.0)hexa-2,5-diene, mouse: 1478

lung or kidney isografts (XVII/G mice), C57BL mice: 1992

6-mercaptopurine, cell-free transmission, mouse: 1552, 2389

methylcholanthrene (mouse): 225, 1228

leukemia virus activation or cell-free transmission: 408, 1552

methylnitrosourea

mouse: 1185, 1935

transplacental, rat: 1876

mineral oil alone or + androgen, mouse: 406, 1175, 1492

mouse leukemia virus, radiation effects, rat: 20

N-(4-[5-nitro-2-furyl]-2-thiazolyl)acetamide, rat: 1510

pesticides, mouse: 31

photographic emulsion component or developing agent, mouse: 2305

polyvinylpyridine N-oxide, mouse or rat: 717

Rauscher mouse leukemia virus, rat: 772

resin intermediates of acetone or phenol production, mouse: 2304

role of thymus, review: 991

saponin, rabbit: 1163

spleen cells inducing graft-host reaction, mouse: 1199

squirrel herpesvirus

marmoset or owl monkey: 513, 2041, 2042

tobacco leaf powder, mouse: 2318

treatments causing runtting syndrome, mouse: 1200

trimethylbenzanthracene, rat: 1829

urethan (mouse): 77, 238, 1080, 1083, 2286

effect of leukemia virus: 2288

virus particles: 75, 408, 1991

viral, leukemia virus cytotropism, review: 1012

LEUKEMOGENESIS, HUMAN (See also Radiation leukemia/lymphoma)

anticonvulsants of hydantoin type: 1909, 1910

benzene, occupational, chromosomes: 951, 952, 1120

or toluene derivatives, occupational: 369, 370, 371, 372

chloramphenicol: 733, 734

griseofulvin: 1201

immunity and genetics, review: 1437

immunosuppressive therapy for kidney

transplants: 2087

phenylbutazone, genetic factors: 1911

treated solid tumors, cases and review: 1727

LEUKEMOID REACTION

Rous sarcoma virus induction, germ-free or conventional rat: 1301, 1953

- LEUKOSIS, AVIAN (See also Marek's disease)
 BAI strain A virus
 properties of non-transforming subgroups: 92
 Marek's disease virus
 review: 2149, 2150
 skin, herpes-type virus particles, chicken:
 1618
- LEUKOSIS, BOVINE
 exposure, leukemia epidemiology, Europe,
 review: 2135
- LEUKOVIRUS (See under Virus, herpes-type)
- LIP NEOPLASMS
 epidemiology
 Canada, urban and rural: 895
 environmental factors, U.S.: 2530
 Italy (Catanzaro and Cosenza Provinces):
 1668
 herpes simplex virus, review: 2147
 premalignant, role of herpes infection or
 injury: 594
- LIPIDS (See also under Fats and Oils, edible)
 analysis, SV40-transformed human cell line
 (WI-38VA13A): 314
 brain tumors, mouse: 1493
 composition, adenovirus 12-induced hamster
 tumors: 1264
 metabolism, breast cancer or fibrocystic
 disease: 938
 plasma membrane, structure and antigenic
 activity, tumor cells: 1429
- LIPOPROTEINS
 serum, rat with induced or transplanted hepatoma:
 1708, 1844
- LIPOTROPES
 deficiency, effect on aflatoxin hepatocarcino-
 genesis, rat: 188
- LIVER
 benzpyrene hydroxylase
 methylcholanthrene induction, rat: 1904
 strain differences, mice: 2205
 carcinogen metabolism, mouse or rat: 184,
 200, 640, 644, 672, 1049, 2235, 2324
 catalase, normal and tumor-bearing rat: 2652
 cholesterol synthesis, effect of aflatoxin,
 rat: 186
 DNA, effect of carcinogens, rat or mouse: 66,
 1066, 1801, 1851, 1872, 1920, 1937, 2244,
 2246, 2256
 enzymes, effect of carcinogenic or noncarcino-
 genic compounds, rat: 379, 1468, 2260, 2310
 free radicals during liver carcinogenesis, rat:
 430
 glycogen, effect of carcinogens, mouse or rat:
 660, 1495, 1531, 1549
 glycolysis and regulating enzymes, effect of
 herbicide, rat: 2263
 growth rate, hepatoma-susceptibility genotype,
 mouse: 2618, 2619, 2620
 hepatocarcinogen toxicity, mechanism, rat:
 1860
 lysosomes, effect of aflatoxin, rat: 670
 microsomes
 effect of
 carcinogens, animal: 81, 180, 205, 642,
 643, 645, 646, 1060, 1061, 1062,
 1090, 1091, 1092, 1114, 1115, 1116,
- LIVER (contd.)
 1173, 1205, 1206, 1207, 1496, 1717, 2204,
 2220, 2240, 2241, 2324, 2326
 non-carcinogenic amine (dimethylaniline),
 rat: 2240, 2241
 mitochondria
 enzymes, effect of Friend or Rauscher
 leukemia virus, mouse: 1634
 specific metabolic abnormalities, α -naphthyl-
 isothiocyante or ethionine hepatoma,
 rat: 1173
 nucleoproteins, effect of methylcholanthrene,
 rat: 2325
 partial hepatectomy, effect on urethan
 metabolism or tumor induction, mouse: 2285,
 2286
 polysomes, effect of aflatoxin, rat: 190
 portacaval shunt, effect on DMBA mammary
 tumors, rat: 1823
 proteins, effect of carcinogens, mouse or rat:
 651, 1179, 1540, 1777, 1851, 2234, 2242
 regeneration
 effect of carcinogens, rat or mouse: 204,
 1204, 1491
 normal or mammary tumor-bearing mouse: 941
 RNA, effect of carcinogens, rat or mouse: 66,
 201, 1176, 1538, 1851, 1920, 1937, 2243,
 2244, 2255
 RNase and RNase inhibitor, leukemic mouse:
 343
 tissue-specific inhibitor of DNA synthesis,
 effect of carcinogens, rat: 1532
 toxicity
 aflatoxin
 chicken: 257, 365
 fish: 665, 666
 human: 1914
 monkey: 1913, 2298
 mouse: 1915, 1938
 rat: 1938
 cycad seeds, chick: 240
 diethylnitrosamine, rat: 1148
 dimethylnitrosamine, dog or monkey: 1871
 food coloring (Ponceau MX), mouse: 609
 pyrrolizidine alkaloid, rat: 2308
 retrorsine, monkey: 2298
 sterigmatocystin, monkey: 2298
- LIVER CARCINOGENESIS
 aflatoxins
 hamster: 187
 mouse: 1938
 rat: 185, 188, 362, 363, 671, 1110, 1111,
 1144, 1938, 2292, 2295
 species difference, salmon or trout: 666
 trout: 418, 665, 1487, 2330
 afutoxin (aflatoxin analog)
 mouse: 1488
 o-aminoazotoluene
 mouse: 1169, 1895
 trout: 418
 avian adenovirus (CELO)
 hamster: 2511
 azobenzene
 compounds, rat: 63, 396, 1890
 benzidinedicarboxylic acid
 rat: 1923

LIVER CARCINOGENESIS (contd.)

carbon tetrachloride
strain difference, rat: 420
cycasin
and aglycone, mechanism, review: 1017
mouse: 2303
dibutylnitrosamine
mouse: 248
dichlorodiaminodiphenylmethane
rat: 1894
dietary carcinogens
animal, review: 1014
diethylnitrosamine
guinea pig: 191, 654, 655, 656
monkey: 62
mouse: 236, 1147, 1547
leukemia virus antigen content: 408
synergism with Motol hepatitis virus:
653
rat: 193, 194, 195, 196, 399, 400, 416,
1149, 1530, 1531, 1534, 1869, 1928
dimethylaminoazobenzene
effect of *p*-hydroxypropiophenone, mouse:
1467
rat: 197, 198, 206, 416, 430, 659, 920,
1137, 1138, 1139, 1140, 1495, 1549,
1885, 1886, 1890, 1940, 2258, 2259,
2261, 2262, 2263, 2264
effect of other carcinogens: 192, 430,
650
rat, review: 2154
transplantable tumor (D23), membrane-
associated tumor-specific antigens:
203
dimethylbenzanthracene
germ-free mouse: 611, 702
dimethylhydrazine
hamster: 1905
dimethylnitrosamine
guinea pig: 1533
mouse: 1185, 1870
rat: 192, 247, 721, 1145
interaction with dimethylaminoazobenzene:
192
trout: 418, 1868
dinitrosopiperazine
mouse: 1883
dioxane
rat: 1160
diphenylpropynyl-N-cyclohexylcarbamate
rat: 1563
ethionine
rat: 1144, 1173, 1847
ethylbutylnitrosamine
rat: 1535
fluorenylacetamide
mechanism, rat, review: 3
mouse: 1843
rat: 61, 416, 430, 671, 1202, 1560, 1842,
1844, 1845, 1846, 1847, 1848, 1852, 1939,
2247, 2248
fluorenyldiacetamide
effect of reserpine, mouse: 1856
pre-malignant, hormone effects, rat: 424
fluorenylenebisacetamide
rat: 1468, 1508, 1857

LIVER CARCINOGENESIS (contd.)

fluorobiphenylacetamide
age and sex difference, rat: 1509
food additives
mouse: 1779
2-(2-formylhydrazino)-4-(5-nitro-2-furyl)
thiazole and related agents
rat: 1548
hexamethylbicyclo(2.2.0)-hexa-2,5-diene
mouse: 1478
high-fat diet
mouse: 250
high-fat/low-protein diet inducing cirrhosis
rat: 673
hydrazine sulfate
sex difference, mouse: 1500
hydroxyfluorenylacetamide
rat: 1852, 1853, 1854, 1855, 2249
tumor susceptibility, species difference,
rodent: 1550
mechanism, theory, human: 2561
methoxyaminoazobenzene
rat: 1889
methylcholanthrene
enzymes, rat: 1902
methyldimethylaminoazobenzene
guinea pig: 199
rat: 395, 651, 652, 1141, 1142, 1143,
1468, 1847, 1887, 1888, 1891, 2154,
2179, 2180
 α -naphthylisothiocyanate
specific biochemical abnormalities, rat:
1173
nitroso compounds
mechanism, review: 998
nitrosomorpholine
rat: 194, 1884
oral contraceptive
rat: 1830
pesticides
mouse: 31
polyoma virus + fluorenylacetamide
synergism, rat: 1202
radiation
mouse: 2178
review: 2118
thioacetamide
rat: 194, 400, 2263
tobacco leaf powder
mouse: 2318
m-toluenediamine
effect of other carcinogens, rat: 2235
s-triazine compounds
mouse or rat: 2272
urethan
effect of leukemia virus, mouse: 2288
partial hepatectomy, mouse: 2286

LIVER DISEASES

cirrhosis
alcoholic, malignant transformation: 1415
dietary, liver tumors, rat: 673
dimethylnitrosamine induction, dog: 2279
oropharynx cancer, U.S.: 1384
cirrhosis with/without hepatoma
epidemiology
Japan, alcohol consumption: 2560

LIVER DISEASES (contd.)

Switzerland (Zurich): 129

hepatitis

associated (Australia) antigen distribution,
leukemia or Hodgkin's disease: 2591

LIVER NEOPLASMS

aflatoxin metabolism: 1113

epidemiology

Africa, dietary pyridoxine deficiency: 770

Bulgaria (southeastern): 522

Congo (Brazzaville): 2514

dietary carcinogens, review: 1014

Ethiopia (Addis Ababa), hepatotoxic
taenicides and dietary mycotoxins: 2084international, environmental factors
(chemical and biological): 2561Japan, cirrhosis and alcohol consumption:
2560

Hiroshima/Nagasaki: 2559

South Africa (Bantu), serum zinc levels:
202

Switzerland, cirrhosis, Zurich: 129

Uganda: 1374

hepatoblastoma, siblings (infants): 131

human, transmission to mouse: 2502

malignant transformation of alcoholic cirrhosis:
1415serum α -fetoprotein, review: 2134LIVER NEOPLASMS, EXPERIMENTAL (See under
Neoplasms, experimental)

LUCKÉ TUMOR (See under Kidney neoplasms)

LUCKÉ VIRUS (See under Virus, herpes-type)

LUNG

asbestos bodies

occupational asbestos or dust exposure:
680

structure and development, hamster: 679

benzpyrene

hydroxylase, effect of trace metals and
asbestos, mouse: 1764

uptake, hamster: 675, 2201

cultures, polyoma- or myxovirus-immunized

hamsters, tumor-inducing capacity: 2462

dimethylbenzanthracene metabolism, rat or
hamster: 675, 1801

effect of

asbestos, review: 1713

methylcholanthrene in vitro, lung tumor-
resistant mouse strain: 2188

embryonic

effect of transplacental carcinogens,
mouse, review: 2128treated with dimethylnitrosamine or
methylnitrosourea, adenomatous prolifera-
tion, organ culture, mouse: 1517urethan or hydroxyurethan cytotoxicity
in vitro, mouse: 2290

enzymes, effect of nickel carbonyl, rat: 2310

mucociliary efficiency, smokers: 1770

postnatal cellular proliferation, urethan
susceptibility, mouse or hamster: 2287

toxicity

beryllium and beryllium-containing rocket
exhaust products, rat: 2312

isoniazid, animal or human: 1159

tobacco smoke, measurement method, mouse:
2317

LUNG CARCINOGENESIS

antitumor agent (ibenzmethylin)
mouse: 605

asbestos

rat: 1101

azapropazone

mouse: 1840

aziridines and carbamates

bioassay method, mouse: 410

benzidinedicarboxylic acid

rat: 1923

benzpyrene

hamster: 1089

mouse: 2199

rat: 1793

transplacental, mouse: 2329

beryllium

rat: 678, 2312

bis(chloromethyl)ether

mouse: 676

cerium hydroxide dust and radon
rat: 2171

chloromethyl methyl ether

mouse: 676

dibutyl nitrosamine

hamster: 1537

mouse: 248

diethylnitrosamine

hamster: 398

mouse: 236, 1147, 1547

dimethacrine

mouse: 1840

dimethylbenzanthracene

mouse: 702, 703, 1039

dimethylnitrosamine

mouse: 1870

dinitrosopiperazine

mouse: 1883

ethylnitrosourea

transplacental, mouse: 1152

food additives

mouse: 1779

formic acid 2-(4-[5-nitro-2-furyl]-2-thiazolyl)
hydrazide

mouse: 1907

human

asbestos, occupational: 1762

therapeutic pneumothorax and/or fluoroscopy
for TB: 1748

hydrazines and related compounds

mouse: 252, 1498, 1499

hydroxyaminoquinoline oxide

rat: 428

isonicotinic acid hydrazide

animal and human, review: 1441

effect of arginine glutamate, mouse: 1499

lead acetate or nitrate

nucleolar abnormalities, frog: 2309

mathematical model, animal: 1559

methylcholanthrene

mouse: 60, 2187, 2199

methylnitrosamines and methylnitrosamides

mouse: 1185

N-(4-[5-nitro-2-furyl]-2-thiazolyl)acetamide
rat: 1510

2-nitroquinoline

mouse: 251

LUNG CARCINOGENESIS (contd.)

- nitroquinoline oxide
 - rat: 674
 - scar tissue, mouse: 1475
- nitrosopiperidine
 - mouse: 67
- ²³⁹Pu
 - rat: 2176, 2177
- radiation
 - mouse: 1749, 1754, 2178
- screening method, newborn mouse: 701
- tobacco
 - leaf powder, mouse: 2318
 - review: 1714, 1715
 - tar, mouse: 1768
- transplacental, mouse: 714
- urethan (mouse): 59, 411, 677, 1039, 1081, 1082, 1083, 1526, 1778, 1838, 1839, 1840, 1841, 2286, 2287
 - associated virus-containing leukemia: 1991
 - effect of
 - influenza virus: 2291
 - leukemia virus, mouse: 2288
 - related compounds, structure-activity relationship: 58
- zinc-dithiocarbamic acid herbicides
 - mouse: 1778

LUNG DISEASES

- asbestosis, asbestos detection: 182, 680
- occupational, lung cancer, Japan: 2320, 2321
- tuberculosis
 - lung cancer, males: 127
 - USSR (Moscow): 2073
 - therapeutic pneumothorax and/or fluoroscopy, risk of breast or lung cancer: 1042, 1748

LUNG NEOPLASMS

- associated
 - dermatomyositis, cases and review: 1704
 - XX/XXY mosaicism (Klinefelter's syndrome), SV40 transformation of WBC and fibroblast cultures: 2456
- bronchogenic carcinoma
 - chromosomes: 684
 - doubling times, review: 1451
 - growth kinetics, mathematical model: 2615
 - nuclear DNA content: 1426
- epidemiology
 - air pollution: 902, 1659, 1699, 2537, 2538, 2543
 - review: 574
 - anesthesiologists, U.S. and Canada: 888
 - blood groups (A, B and H antigens) and mixed-cell agglutination reaction: 2626
 - California (San Diego), smoking, sex difference: 2541
 - Canada: 894
 - diabetic or nondiabetic men: 541
 - East Germany, air pollution and smoking: 2543
 - England and Wales, coal mining and textile-manufacturing areas, air pollution: 1660
 - Finland (Helsinki): 903
 - Hungary (Szeged), smoking: 1654
 - Iceland, smoking: 1653
 - Italy: 327, 994

LUNG NEOPLASMS (contd.)

- smoking: 325
- Japan
 - occupational pneumoconiosis with/without asbestosis: 2320, 2321
 - urban, air pollution and smoking: 1657, 2538
- Massachusetts, diabetes mellitus: 2519
- Montreal, smoking, Jews: 2539
- occupational radiation exposure: 1755
- Pennsylvania (Pittsburgh), smoking, Jews: 2540
- Poland, urban and rural: 529
- review: 532, 994
- risk of second primary tumor, New York: 1665
- Scotland
 - coal miners, smoking: 1659
 - urban and rural, air pollution and smoking: 2536
- smoking: 128, 179, 325, 901, 904, 928, 1337, 1653, 1654, 1655, 1657, 1659, 1748, 2536, 2538, 2539, 2540, 2541, 2542, 2543
 - review: 166, 569, 574, 1024, 1714, 1715
- solid fuel exposure, international: 179
- South Africa
 - doctors and dentists, ethnic groups, smoking: 1655
 - smoking, ethnic groups: 901, 928, 2542
- U.S., smoking: 1337
- Utah: 1351
- West Germany, appendectomy: 2587
- familial, age-, sex- and site-related patterns: 1679
- growth rate, mathematical model: 946
- lung scar cancer, pathology: 1043, 1044
- malignancy-associated chromatin changes, peripheral neutrophils: 949
- metastatic, growth rates: 539
- mouse
 - strain differences: 983, 2643
- serum and tissue cadmium and zinc: 1135
- tuberculosis
 - isoniazid-treated pt. group: 1159
 - risk of cancer, males: 127
 - therapeutic fluoroscopy and/or pneumothorax, smoking: 1748
- USSR (Moscow): 2073
- LUPUS ERYTHEMATOSUS, SYSTEMIC (See under Immunity disorders)
- LUTEOSKYRINE
 - effect on DNA and chromosomes, tumor cells: 1172
 - food contamination, review: 366
- LYMPH NODES
 - follicular hyperplasia, rheumatoid arthritis: 340
 - non-lymphomatous hyperplasia, leukemia virus-like particles, human: 1233
- LYMPHATIC SYSTEM NEOPLASMS
 - metastatic, growth rates, human: 539
- LYMPHATIC TISSUE
 - mast cell proliferation, age-related, NZB mice: 1706
 - methylnitrosourea toxicity, mouse: 1557

LYMPHATIC TISSUE (contd.)

pathology, Rauscher viral leukemia, mouse: 2349

LYMPHOMA, MALIGNANT, EXPERIMENTAL

bovine lymphosarcoma

nuclear ultrastructure: 470

transplantability, effect of antilymphocyte serum, calf: 469

canine

cellular transmission: 2112

mast cell tumor, virus-like particles: 282

transmissible venereal tumor, possible

viral etiology, review: 357

epidemiology

farm animals, U.S.: 1691

reticulum cell sarcoma outbreak, leukosis- and lymphoma-free Japanese quail colony, Hawaii (Honolulu): 2051

Wistar rats: 732

feline

isolation and properties of syncytium-forming virus: 448

leukemia virus antigens, lymphosarcoma,

cats, dogs and other animals: 447

virus-induced lymphosarcoma, pathology: 1964

Friend virus-induced

pathology, disappearance of virus, mouse: 98

rat, pathology: 100

reticulum cell sarcoma, loss of virus

in vitro, mouse: 106

FVTCT reticulum cell sarcoma (mouse)

recovery of Friend leukemia virus: 769

Gross leukemia virus

host immunity, mouse: 763

thymus graft from infected mouse: 1646

induction

cycasin

mouse: 2303

dimethylbenzanthracene

hamster: 74

mouse: 377, 2389

dimethylnitrosamine

mouse: 402

echovirus-12 or reovirus-3 (human)

hamster: 518

6-mercaptopurine

alkaline phosphatase, mouse: 2389

cell-free passage, mouse: 1552

methylcholanthrene

cell-free passage, mouse: 1552

methylnitrosourea

mouse: 1935

radiation

germ-free or conventional mice: 589

rat-adapted erythroblastosis virus

extrathymic lymphomas, rat: 753

spleen cells inducing graft-host reaction

mouse: 1199

squirrel herpesvirus

marmoset or owl monkey: 513, 2041, 2042

treatments causing runtting syndrome

mouse: 1200

2731/L (mouse)

from reovirus-infected mouse, association

with Gross-AKR type leukemia virus: 757

LYMPHOMA, MALIGNANT, EXPERIMENTAL (contd.)

Moloney leukemia virus-induced

splenic antibodies, mouse: 770

Mycoplasma neurolyticum-infected mice: 1232

NZB mice

effect of germ-free status: 1430

oil-induced

cloning efficiency and karyotype, mouse: 2640

radiation leukemia virus (rat)-induced

virus particles and antigenicity, rat or mouse: 1628, 1636

radiation- or carcinogen-induced

possible leukemia virus, mouse: 408, 1203

Rauscher leukemia virus-induced

mouse: 771, 774

pathology, rat: 772

SJL/J mouse reticulum cell sarcoma

growth kinetics, theoretical model: 2050

⁹⁰Sr-induced

pathology, swine: 26

TM reticulum cell sarcoma (hamster)

cellular transmission, insect vectors: 555

LYMPHOMA, MALIGNANT, HUMAN

associated

congenital hypogammaglobulinemia, case (child) and review: 2107

systemic lupus erythematosus and dysgamma-globulinemia, case and review: 2639

Burkitt's

cells and cell lines, properties: 84, 86, 829, 831, 1257, 1614, 1617, 1643, 2036, 2061, 2114, 2479, 2663

cell-transmitted mouse leukemia, properties: 1228

epidemiology

Japan and Okinawa: 1671

Kenya (western) and Tanzania (north-western): 2520

review: 355

Uganda

clustering, West Nile District: 133

possible association with endemic

malaria, West Nile District: 878

sickle cell trait genotype, Kampala: 2609

Epstein-Barr virus

detection methods: 827, 828, 830

review: 1443, 2138, 2148

serum antibodies: 87, 826

children, Africa: 509

intracellular and membrane antigen

complexes: 2039

Japan and Taiwan: 2038

serum antigens: 2481

karyotype: 158, 341

properties of transfer RNA: 2029

reovirus Type 3, review: 2138

virus-like particles, biopsy specimens: 2478

chromosomes, review: 2151

epidemiology

abdominal lymphomas, children, Israel,

ethnic groups: 2610

anesthesiologists, U.S. and Canada: 888

chemists, U.S.: 933

LYMPHOMA, MALIGNANT, HUMAN (contd.)

- high-risk associated disorders (immunity deficiencies), review: 585
- Iran: 2092
- Jamaica, comparison with Africa: 2608
- leprosy, U.S.: 880
- New York, occupational asbestos exposure: 1763
- review: 1016
- Saudi Arabia (Dhahran), environmental factors: 2091
- West Germany: 2607
- Epstein-Barr virus
 - cell lines, properties: 1615, 2631
 - serum antibodies, normal children or adults: 1616
 - isolation, properties and geographical distribution: 1255
 - serum antibodies, tumors other than Burkitt's lymphoma: 509
 - West Germany (Essen): 2037
- familial, Nebraska: 1333
- Hodgkin's disease
 - cell growth kinetics: 536
 - cell lines, properties: 267, 299
 - DNA induction of virus formation, HeLa cells: 1294
 - epidemiology
 - children, Brazil (São Paulo): 1681
 - hepatitis-associated (Australia) antigen distribution: 2591
 - Israel, ethnic groups: 1696, 1697
 - review: 532
 - West Germany: 2606
 - worldwide: 524, 1726
 - radiation-induced myeloid leukemia, chromosomes: 1405, 1460
 - relationship to multiple sclerosis, review: 2139
 - seasonal variations, Germany (Göttingen): 525
 - virus isolation and properties: 85
- hydantoin anticonvulsants: 1909, 1910
- immunity, review: 16
- lymphocyte cultures, chromosomes: 2638
- lymphosarcoma
 - cell line, ultrastructure: 978
 - feline leukemia virus antigens: 447
- occupational radiation exposure: 1755
- pathogenesis, DNA, RNA and enzyme histochemistry, review: 1438
- reticulum cell sarcoma
 - herpes-type virus-positive WBC, surface characteristics: 1614
 - radiation-induced: 1745
- serum SV40 antibodies, children: 1605
- small intestine, epidemiology, Michigan (Detroit): 2553
- virus etiology, review: 2146

MALARIA

- mouse, effect on Harvey viral sarcoma: 1960
- possible association with Burkitt lymphoma, Uganda (West Nile district): 878

MALIGNANT TRANSFORMATION

- achalasia of cardia or chemical burn to cancer of esophagus: 360, 1457, 1741, 2159, 2160
- alcoholic cirrhosis to carcinoma of liver: 1415
- benign or epithelial nevus to melanoma: 558, 2671
- brain injury to brain tumor, child: 1738
- calcifying Malherbe's epithelioma of skin, case: 2657
- carcinogen-induced, hamster embryo cells: 1553, 1561
- cholelithiasis to gallbladder cancer: 130, 899
- chronic inflammation to cancer of pancreas, Germany (Heidelberg): 521
- dental prosthesis irritation to cancer of hard palate: 1739
- endometriosis of rectovaginal septum to adenoacanthoma: 144
- epidermodysplasia verruciformis to carcinoma of skin, verruca vulgaris virus particles, case: 2501
- esophageal or pharyngoesophageal diverticulum to cancer of esophagus: 1000, 2669, 2670
- familial polyposis
 - cancer of colon: 336, 964, 1332, 2103, 2558, 2672
 - (Peutz-Jeghers), stomach cancer, child: 962
- fibroadenoma to malignant cystosarcoma phyllodes of breast: 2668
- fibrous dysplasia to sarcoma of bone: 339
- gastrectomy or gastroenterostomy, esophagus cancer: 1045
- hereditary skin diseases, human: 1742
- hidradenitis suppurativum to carcinoma of skin: 1417
- idiopathic megaesophagus to cancer of esophagus: 961
- injury or herpes infection to premalignant or malignant lip neoplasms: 594
- irradiated lymph node to reticulum cell sarcoma: 1745
- lupus vulgaris to skin cancer, sun exposure or radiotherapy: 595
- lymphocyte cultures
 - blastoid transformation, significance, review: 560
 - chronic lymphocytic leukemia: 1423
 - mongolism: 1402
 - normal persons: 1414
- mechanism, review: 12, 13, 1006, 1450
- megaesophagus to cancer of esophagus: 961
- methylcholanthrene-exposed mouse prostate culture: 226, 1065
- mouse embryo cells, karyotype, effect of culture medium: 346
- Paget's disease of bone, sarcoma at site of injury: 1404
- peptic ulcer to stomach cancer: 596, 939
- radiation
 - cure of tracheal cancer, esophagus cancer: 593

MALIGNANT TRANSFORMATION (contd.)

- dermatitis to skin cancer: 1740, 1743
- rat embryo cell cultures, nitroquinoline oxide: 1166
- regional enteritis to cancer of small intestine: 1410
- risk
 - cold nodules to carcinoma of thyroid: 1705
 - large intestinal or bladder polyps, review: 1449
- scar tissue
 - lung cancer, pathology, human: 1043, 1044
 - phagedenic or rodent ulcer, skin cancer: 24, 332, 988, 2666
 - skin cancer: 1458, 1740, 1745, 2158, 2162, 2666
- scleroderma, case (bronchial cancer) and review: 2153
- spontaneous
 - germ-free rat embryo cells: 1296
 - mouse prostate cell cultures: 348
 - mouse, rat or hamster embryo cell cultures: 977, 979, 981
 - rat embryo cell cultures, karyotype: 2628
- streptokinase-exposed lymphocytes, age factors, human: 1702
- SV40 or polyoma virus, mechanism, review: 10
- syphilis to cancer of penis: 1401
- systemic lupus erythematosus to acute leukemia: 337
- therapeutic pneumothorax and/or fluoroscopy (for TB), lung cancer risk: 1748
- ulcer resection site to carcinoma of stomach, risk, Hungary or Poland: 358, 359
- vaginal
 - pessary implantation, vaginal adenocarcinoma: 1456
 - reconstruction (cervix cancer surgery), primary carcinoma of artificial vagina: 2658

MAMMARY CARCINOGENESIS, EXPERIMENTAL (See also

- Virus, mammary tumor)
 - abnormal estrogen balance, rat, review: 1
 - 5-acetamido-3-(5-nitro-2-furyl)-6H-1,2,4-oxadiazine
 - rat: 427
 - N-acylarylhydroxylamines
 - structure-activity relationship, rat: 2251
- alkylnitrosoureas
 - pregnant rat: 713
- aminophenanthrene derivatives
 - rat: 246
- benzidine
 - rat: 2233
- butyl carbamate
 - mouse: 712
- detergent additives (acenaphthenes)
 - mouse or rat: 1772
- diethylstilbestrol
 - virus-like particles, rat: 2000
- 1-(4-dimethylaminobenzal)indene
 - rat: 53
- dimethylaminobiphenyl
 - LDH isozymes, rat: 55
- dimethylbenzanthracene
 - mouse: 210

MAMMARY CARCINOGENESIS, EXPERIMENTAL (contd.)

- mammary tumor virus-free, low-spontaneous
 - mammary tumor strain: 1253
 - virus-free preneoplastic nodules: 1836
- rat: 44, 54, 56, 57, 212, 219, 376, 649, 708, 709, 711, 920, 938, 1041, 1070, 1071, 1558, 1821, 1822, 1823, 1824, 1825, 1898, 2226, 2227, 2228
- virus-like particles: 2000
- diphenylpropynyl-N-cyclohexylcarbamate
 - rat: 1563
- DNA from mouse tumor
 - virus-positive tumors, mouse: 419
- estradiol + pituitary graft
 - hyperplastic nodules, effect of nodule-inducing or mammary tumor virus, mouse: 286
- estrogens or estrogen + progestagen combinations
 - review: 2
- ethylnitrosourea
 - mouse: 2282
- ethylsulfonylnaphthalene-1-sulfonamide
 - mouse: 724
- fluorenylacetamide
 - rat: 417
- formic acid 2-(4-[5-nitro-2-furyl]-2-thiazolyl)hydrazide
 - mouse: 1907
- 2-(2-formylhydrazino)-4-(5-nitro-2-furyl)thiazole and related agents
 - rat: 1548
- hydrazinethiazole compounds
 - rat: 1906
- hydroxyaminoquinoline oxide
 - rat: 428
- mammary tumor virus + hormones
 - effect of thymectomy, mouse: 820, 821
- methods, mouse: 289
- methylcholanthrene (rat): 394, 1898
 - virus-like particles: 2000
- methylnitrosourea
 - transplacental, rat: 1876
- 5-nitrofurans derivatives
 - rat: 417
- N-(4-[5-nitro-2-furyl]-2-thiazolyl)acetamide
 - rat: 1510
- oral contraceptive
 - rat: 1830
- pituitary graft
 - rat: 1504
- polyvinylpyridine N-oxide
 - mouse or rat: 717
- radiation
 - mouse, methods: 289
 - virus-free preneoplastic nodules: 1836
- rat: 1746
- trimethylbenzanthracene
 - rat: 1829
- urethan (mouse): 712, 1836
- viral or chemical
 - epithelial-mesenchymal junction ultra-structure, mouse: 349

MAMMARY CARCINOGENESIS, HUMAN

- benign fibroadenoma, oral contraceptives: 1126, 1806, 1831

MAMMARY CARCINOGENESIS, HUMAN (contd.)

- diethylstilbestrol, male: 1834
- estrogen-progestagen contraceptives: 1125
- radiotherapy for mastitis, New York (upstate): 23
- therapeutic pneumothorax with fluoroscopy (for TB): 1042

MAMMARY GLAND

- dimethylbenzanthracene uptake, rat: 1212, 1826
- DNA, effect of benzanthracene or dimethylbenzanthracene, hormone effects, rat: 1069, 1523

- growth kinetics, estrus cycle, rat: 2616

MAMMARY NEOPLASMS, EXPERIMENTAL (See also Virus, mammary tumor)

- Adenocarcinoma 755 (mouse)
 - mammary tumor virus particles: 2395
- dimethylbenzanthracene-induced, isolation of mammary tumor virus, rat: 1598
- effect of immunosuppression, syngeneic or allogeneic host-tumor systems, mouse: 2627
- genotypic mosaicism, allophenic mice: 159
- hyperplastic alveolar nodules
 - DNA, effect of oophorectomy or mammary tumor virus, mouse: 1623
 - effect of
 - mammary tumor or nodule-inducing virus, mouse: 819
 - methylcholanthrene, mouse: 819
 - frequency, high- or low-nodule-inducing virus mouse sublines: 1622
 - hormone effects, mouse: 710, 819
 - liver regeneration pattern, mouse: 941
 - loss of estradiol binding, mouse: 155
- male mouse, estrogen-producing Sertoli cell + interstitial cell tumor of testis: 152
- mammary tumor virus
 - immunity, mouse: 285
 - replication and ultrastructure, mouse: 816, 817, 1594
- mouse cell line, stimulation of virus production, tissue culture and newborn mouse or rat: 1597
- nodule-inducing virus detection, mammary tumor virus-free, high-tumor mouse strain: 1599
- occurrence, strain differences, mouse: 554, 983, 1253, 1712
- pathology, NZB mice: 291
- rat tumor induced by Moloney sarcoma virus, pathology: 2368
- risk, effect of spaying, dog: 969
- S3C carcinoma (mouse)
 - spontaneous, immunogenicity, mouse: 1248
- spontaneous
 - epidemiology, dogs, USSR (Moscow), genetic factors: 2098
 - immunogenicity, virus-free mice: 2053
 - incidence, effect of estrogen-protestagen contraceptives, mouse: 1503
 - mouse, properties of DNA: 2648
 - plasma prolactin, rat: 728
 - role of virus, PBA mouse strain: 2643
 - transplantability, role of connective tissue, mouse: 2646
 - virus particles, cat: 1644

MAMMARY NEOPLASMS, EXPERIMENTAL (contd.)

- transfer RNA-methylating enzymes, mouse or rat: 2647
- transmission
 - high- to low-tumor mouse strain, foster-nursing: 1642
 - virus-positive to virus-free mouse strains: 1997
- transplantable
 - effect of
 - immune sera, mouse: 623, 1472
 - radiation or mammary tumor virus, mouse: 28
 - fibrinogen metabolism, mouse: 974
 - prolactin- or growth hormone-enhanced, mechanism, mouse: 2267
 - psychokinetic effects, mouse: 985
 - virus structures, mouse: 476
- MAMMARY NEOPLASMS, HUMAN
 - benign fibroadenoma
 - malignant transformation (cystosarcoma phyllodes): 996
 - oral contraceptives: 1806, 1831
 - epidemiology: 912, 2563
 - age factors, international: 1388
 - Canada: 894
 - chemists, U.S.: 933
 - contraceptives, review: 2, 557
 - endocrinology: 335
 - England and Africa (Nigeria and Uganda), comparison of malignancy, genetic factors: 2562
 - environmental temperature, geographical variations, U.S.: 1343
 - ethnic groups, Oklahoma: 1353
 - Greece (Athens), reproductive histories and lactation: 2079
 - hormone metabolism, review: 1, 583, 1724, 1725
 - identification of high-risk groups, review: 582
 - India (Bombay), Hindus and Parsis: 2066, 2067
 - infants and children, Canada (Ontario): 1346
 - irradiated postpartum mastitis, upstate New York: 23
 - Japan
 - leukemia incidence after radiotherapy: 2168
 - relationship to leukemia incidence: 2601
 - reproductive history and lactation: 2566
 - lactation and reproductive histories, international: 1356, 1385, 2079, 2565, 2566, 2567
 - males
 - Finland: 1379
 - Klinefelter's syndrome: 1400
 - Massachusetts (Boston), reproductive histories and lactation: 1356
 - Minnesota (Minneapolis): 1344
 - New York City: 2564
 - pre- and postmenopausal patterns, Germany (Berlin): 2080
 - pulmonary fluoroscopy for TB: 1042
 - review: 532, 1723

MAMMARY NEOPLASMS, HUMAN (contd.)

Taiwan, reproductive histories: 2567
 Utah: 1687
 Wales (southern), reproductive histories:
 1385

estradiol binding capacity, benign or
 malignant tumors: 1505
 frequency of pituitary metastases: 966
 growth kinetics: 538, 2100, 2612
 herpesvirus-like particles: 2044
 hormone excretion and psychological factors:
 1412
 incidence, women with salivary gland tumors:
 338
 lipid, enzyme and nucleic acid histochemistry:
 938
 malignant or preinvasive, karyotype: 342
 risk of second primary tumor, Connecticut:
 909
 serum adenovirus-18 antibodies: 834
 sex chromatin: 955
 tumor extracts, lymphocyte transformation,
 normal subjects and breast cancer: 546
 virus-like particles: 293, 294, 295, 1600

MAREK'S DISEASE (See also under Virus, herpes-type)

CAL-1 strain, properties of virus: 91
 cell-free transmission, chick: 2486
 serum immunoglobulins, chicken: 1258
 virus
 antigen localization, host genetics,
 chicken: 508
 etiology, review: 2149, 2150
 specific antigens and cell-free virus,
 infected or tumor-bearing chickens: 2484

MAREK'S DISEASE VIRUS (See under Virus, herpes-type)

MARIHUANA (See Cannabis)

MAST CELL TUMOR, CANINE (See under Lymphoma, malignant, experimental)

MELANOMA, MALIGNANT

chromosome abnormalities: 1393
 epidemiology
 Australia, geographical variations, sun
 exposure: 1381
 Switzerland: 2076
 U.S., age factors: 2528
 familial (3 generations): 2077
 genetics, review: 1718
 hamster
 virus-like particles: 82, 1996
 identical twins: 1330
 intranuclear virus-like inclusion bodies,
 human: 1292
 transplantable (mouse or hamster)
 separation of viable tumor cells: 2645

MELATONIN

effect on dimethylbenzanthracene mammary
 tumors, rat: 1041

6-MERCAPTOPURINE (See also under Antitumor agents)

thymic lymphoma, viral transmission, enzymes,
 mouse: 1552, 2389

MESIDINE

toxicity, lung, mouse: 701

METABOLISM (glycolysis and respiration)

dimethylbenzanthracene-induced tumors, mouse:
 649, 1521

METABOLISM (contd.)

effect of hepatocarcinogens, rat liver:
 1138, 2262, 2263
 high- and low-tumor-producing mouse cell
 clones: 345, 347
 Krebs cycle metabolites, stimulation of tumor
 cells in vitro: 615

METABOLISM DISORDERS

diabetes mellitus and glucose-6-phosphate
 dehydrogenase variants, genetic and cancer
 susceptibility: 541

METALS, HEAVY

analysis
 cigarette tobacco and smoke (filtered or
 unfiltered): 686
 carcinogenesis, human, review: 996
 trace
 analysis, human tumors: 1934
 drinking water, cancer incidence, Italy
 (Pesaro): 2072
 effect on benzpyrene hydroxylase, mouse
 lung: 1764

METAPROTERENOL

effect on tobacco smoke-induced ciliostasis,
 rabbit trachea in vitro: 2323

METHANESULFONATE, METHYL-

effect on RNA, rat liver: 1157
 mutagenesis, Neurospora: 1158

METHENAMINE

toxicity, rat: 1922

METHOTREXATE (See under Antitumor agents)

METHYLAZOXYMETHANOL (See Cycasin aglycone)

3-METHYLCHOLANTHRENE

benzpyrene hydroxylase induction, rat liver or
 hepatoma: 1904
 binding to chromatin or DNA, rat liver: 1066
 brain tumors
 mouse: 1048, 1051, 2189
 virus-like particles: 822, 1297,
 1567, 1621
 rat: 234

carcinogenic effect, hamster strain (Phodopus
sungorus): 2642

cervix tumors, rat: 707

chimera induction, irradiated rat: 1046

effect on

aromatic hydrocarbon breakdown, rat liver:
 1049

cytochrome P-420, rat liver: 2326

dimethylbenzanthracene metabolism, rat
 liver microsomes: 2220

Goldblatt-type hypertension, rat: 2193

immunity, mouse: 614

liver microsomes, animal: 645, 1060, 1061,
 1062, 1091, 1496

lung explants from lung tumor-resistant
 mouse strain: 2188

nucleoproteins, rat liver: 2325

protein synthesis, human WBC: 1192

RNA transcription, rat liver: 1208

Rous virus tumors, chick: 52

serum hemopexin, rabbit: 1903

m-toluenediamine liver tumors, rat: 2235

tumor development, transplanted hyper-
 plastic alveolar mammary nodule, mouse:
 819

3-METHYLCHOLANTHRENE (contd.)

epidermal tumors, amphibia (Bufo arenarum): 1056
 immunosuppression, mouse: 393, 1511
 intestinal absorption, mechanism, animal: 1213
 leukemia, mouse: 1228
 liver tumors, rat: 1902
 lung tumors, mouse: 60, 2199
 lymphoma (mouse): 225
 cell-free passage, mouse: 1552
 leukemia virus activation: 408
 mammary tumors (rat): 349, 394, 1898
 virus-like particles: 2000
 mechanism of action, review: 2155
 metabolism, rat liver: 1205, 1206, 1207
 muscle tumors
 circadian changes of body temperature, liver catalase and plasma iron, rat: 2652
 mouse: 2191
 transplanted, fibrinogen metabolism, mouse: 974
 neoblastic tumors, planaria: 627
 osteosarcoma, rat: 2198
 ovarian tumors, rabbit: 1047
 photodynamic effect, Neurospora or hamster cells: 1804
 premalignant epidermal hyperplasia, mouse skin: 1188
 prostate tumors, rat: 390, 716, 1052
 rhabdomyosarcoma (MCG1-SS), effect of anti-coagulants, mouse: 1469
 sarcoma, immunogenicity, mouse: 1248
 s.c. tumors
 attempted induction, cattle: 1068
 squirrel monkey: 700
 guinea pig: 657
 mouse: 40, 41, 42, 43, 51, 391, 611, 658, 1063, 1064, 1472, 1512, 1514, 1515, 1516, 1541, 1900, 2183, 2196, 2348
 rat: 1502, 2190, 2192, 2194, 2348
 skin tumors
 mouse: 48, 222, 223, 224, 256, 389, 391, 392, 393, 537, 1054, 1055, 1057, 1058, 1067, 1078, 1463, 1486, 1565, 2156, 2182, 2184, 2191, 2195, 2197
 virus-like particles: 1896
 rat: 659, 707
 solid or ascites tumors, chromosomes, rat: 1053
 soluble tumor antigens, delayed hypersensitivity reaction, guinea pig: 415
 specific carcinogen-binding skin protein, mouse: 2221
 stomach tumors
 guinea pig: 1899
 mouse: 2191
 thyroiditis, rat: 1050
 toxicity, insect (cockroach): 624
 transformation
 hamster embryo cells: 1553
 mouse prostate cells: 226, 388, 1065
 transformed cells
 lung cultures, s.c. tumors, ultrastructure, mouse: 1897

3-METHYLCHOLANTHRENE (contd.)

mouse prostate, transplantation antigens: 2185
 transplanted tumors karyotype
 hamster: 221
 mouse, properties: 622, 1059, 1209
 tumor induction in s.c. lung transplants, mouse: 1462, 2187
 uterine tumors, mouse: 1901
 METHYLHYDRAZINE COMPOUNDS
 chromosomal abnormalities, review: 1716
 6-METHYLMERCAPTOPYRINE RIBONUCLEOSIDE (See under Antitumor agents)
 METOPIRONE
 immunosuppression, chronic runt disease, tumor incidence, rat: 556
 MITOMYCIN C (See under Antitumor agents)
 MITOSIS (See also Cell growth kinetics)
 cell cycle times, rat hepatomas of different growth rates: 1694
 MITOSIS
 synchronization
 effect on Rous sarcoma virus replication: 1941
 mathematical model, tumor cells: 942
 MONOCROTALINE
 liver toxicity, rat: 2308
 MONURON (See Urea, 3-(p-chlorophenyl)-1,1-dimethyl-)
 MOTION, ROTATORY (See under Stress)
 MOUTH
 intraoral fluid cell metabolism, effect of smoking, human: 413
 MOUTH NEOPLASMS
 betel chewing, case: 2313
 enzymes, human: 373
 epidemiology
 Canada, comparison with other nations: 895
 India ethnic groups, tobacco chewing: 2531
 smoking and tobacco chewing: 935
 Natal (Durban), betel chewing, ethnic groups: 1656
 Papua/New Guinea, betel chewing: 693, 2532
 Poland (Cracow): 528
 Puerto Rico, smoking and dietary factors: 932
 screening methods, review: 990
 hard palate, dental prosthesis: 1739
 multiple primary type, epidemiology, smoking: 931
 pigmented epithelial tumor of maxilla, infant, ultrastructure: 1419
 risk, second primary tumor, New York: 1665
 MUCOPOLYSACCHARIDES
 distribution, polyoma virus-induced hamster sarcoma: 862
 MULTIPLE SCLEROSIS
 relationship to Hodgkin's disease, review: 2139
 MUSCLE
 cultures, differentiation, effect of dimethylbenzanthracene, rat: 2222
 MUSCLE NEOPLASMS (See under Connective tissue neoplasms)

MUTAGENESIS

- aflatoxin B1, bacteria: 364
- alkylating carcinogens, Neurospora: 1158
- aminofluorene and naphthalene compounds, bacteria: 1183
- azobenzene or benzanthracene carcinogens, Drosophila: 1182
- chemical carcinogens, Drosophila: 1760
- chemical screening method, mouse: 1555
- dimethylbenzanthracene, Drosophila: 382
- N-hydroxy-aromatic amide esters, bacteria: 2239
- hydroxylamine, bacteria: 2252
- nitroquinoline oxide, bacteriophage: 1862
- 1-nitroso-2-imidazolidone, Saccharomyces: 742
- nitrosourea compounds, structure-activity relationship: 741
- phthalate compounds and other agents, Drosophila: 626
- radiation, Rous sarcoma virus (Schmidt-Ruppin strain), chick embryo: 2381
- Rous sarcoma virus or SV40, Drosophila: 517
- urethan metabolites, Drosophila: 2289
- Mycoplasma
 - infection, effect on SV40-transformed cells: 2510
- Mycoplasma neurolyticum
 - infection, leukemia frequency, mouse: 1232
- MYCOTOXINS (See under Fungi)
- MYELOFIBROSIS (See under Bone marrow diseases)
- MYELOMA AND RELATED DISEASES
 - cell lines
 - chromosomes, human: 2663
 - cloning efficiency, chromosomes and herpes-type virus: 2631
 - chromosomes, human, review: 2151
 - epidemiology
 - Jamaica: 132
 - Japan, myeloma globulin types, comparison with New York (white and Negro) group: 915
 - Minnesota (Olmsted County): 1349
 - review: 14
 - frog plasmacytoma
 - virus-like particles: 2496
 - MOPC-31B mouse myeloma
 - myeloma protein synthesis in vitro: 1428
 - MPC-37 or MOPC-104E plasmacytoma (mouse)
 - stimulation, antithymocyte serum: 1197
 - mouse plasmacytoma
 - adjuvant-induced, leukemia virus-like particles: 1298
 - cloning efficiency and karyotype in vitro: 2640
 - host immunity, possible latent leukemia virus: 973
 - incidence, high-tumor (PBA) mouse strain: 2643
 - mineral oil-induced: 1492
 - germ-free mice: 1175
 - leukemia virus-like particles: 1250, 1251
 - mammary tumor virus-like particles: 730
 - virus-like particles: 1988
 - plasmacytoma, associated solid tumors, cases and review: 1727

- NAPHTHALENE, N-ACETOXY-1-ACETYLAMINO-
 - mutagenesis (bacteria) and skin tumor-initiating effect (mouse): 1183
- NAPHTHALENE, N-ACETOXY-2-ACETYLAMINO-
 - mutagenesis (bacteria) and skin tumor-initiating effect (mouse): 1183
- NAPHTHALENE, N-HYDROXY-1-AMINO-
 - mutagenesis (bacteria) and skin tumor-initiating effect (mouse): 1183
- NAPHTHALENE, N-HYDROXY-2-AMINO-
 - mutagenesis (bacteria) and skin tumor-initiating effect (mouse): 1183
- NAPHTHALENE-1-SULFONAMIDE, 4-ETHYLSULFONYL-
 - bladder tumors
 - mouse: 724, 993, 2253
 - rat: 2254
 - effect on bladder cell growth rate, mouse: 1167
 - mammary tumors, mouse: 724
- α -NAPHTHOFILAVONE
 - effect on cytotoxicity and metabolism of carcinogens, normal cells: 409
- NAPHTHOL COMPOUNDS
 - carcinogenic or noncarcinogenic, free radical formation, organic solvents or water: 598
- α -NAPHTHYLAMINE
 - metabolism, dog: 69
- β -NAPHTHYLAMINE
 - binding, DNA, RNA and protein, mouse liver or kidney: 1851
- β -NAPHTHYLAMINE
 - bladder tumors
 - dog: 722, 2236
 - rabbit: 1850
 - metabolism, dog: 69
 - occupational exposure, bladder cancer, U.S.: 545
 - proximal bladder carcinogens, dog or human: 4
- NAPHTHYLAMINE COMPOUNDS
 - bladder carcinogenesis, mechanism, review: 1440
 - carcinogenic or noncarcinogenic, free radical formation, organic solvents or water: 598
 - reagents for bacterial nitrate reduction: 1773
- NASAL CAVITY NEOPLASMS
 - dioxane induction, rat: 1160
 - snuff taking, historical review: 2115
- NASOPHARYNX NEOPLASMS
 - cultures, herpes-type virions, Hong Kong (Chinese): 1632
 - epidemiology
 - Chinese, California: 2075
 - review: 1719
 - East Africa, serum Epstein-Barr virus antibodies: 523
 - England, occupational dust exposure (shoe manufacturing and baking) and snuff taking, Northamptonshire: 1658
 - genetic and environmental factors, review: 568
 - Hong Kong (Chinese), virology: 523, 825
 - occupational, review: 1004
 - sinapylaldehyde exposure, international, review: 1004

NASOPHARYNX NEOPLASMS (contd.)

- South Vietnam, environmental and genetic factors: 330
- Taiwan and Japan, serum Epstein-Barr virus antibodies: 2038
- Epstein-Barr virus
 - review: 1443
 - serum antibodies: 523, 826, 925, 2038, 2039
 - serum antigens: 2481

NEOPLASMS, EXPERIMENTAL

- Adenocarcinoma #755 (mouse)
 - mammary tumor virus particles: 2395
- adenovirus 12-induced (hamster)
 - DNA or lipid composition: 1263, 1264
- amphibian tumors (frogs and newts)
 - isolation and properties of cytoplasmic virus: 2497
- angioepithelial tumor of flounder
 - pathology: 153
- benzpyrene-transformed cells
 - hamster sarcoma: 385
- bovine papilloma virus-induced
 - pathology, cattle, horses and rodents: 1269
- BP8 tumor (mouse; carcinogen-induced)
 - effect of anticoagulants: 2302
- C3H tumor (mouse)
 - effect of antilymphocyte serum, syngeneic tumor-host system: 146
- D23 hepatoma (rat)
 - membrane-associated tumor-specific antigens: 203
- Dr-Sd melanoma (fish)
 - effect of amino acids on DNA: 334
- effect of physical or psychological stress, review: 1711
- Ehrlich carcinoma (mouse)
 - ascites or solid, growth patterns: 137, 138
 - cells, bioassay of tobacco smoke: 1545
 - dimethylbenzanthracene binding: 1805
 - effect of carcinogens on DNA: 1172, 1865, 1866
 - growth kinetics, protein synthesis: 1701
 - hyperdiploid or hypotetraploid, hormone effects, sex difference: 1507
 - virus-induced fusion with L cells, properties and malignancy (mice) of hybrid cells (LE strain): 2499
- epidemiology
 - colony of Myiostomys albicaudatus (African white-tailed rats): 1692
 - dogs, USSR (Moscow): 2098
 - effect of phthalate compounds and other agents, Drosophila: 626
 - hamster strain (Phodopus sungorus): 2642
 - mammary tumor virus-free mouse strain (RilleB/DE): 554
- Friend virus-infected cell lines
 - host immunity, rat: 764
- GA hepatoma (Marek's disease-associated) (chicken)
 - transfer RNA methylase, chick: 1319
- genetics, review: 1436
- germ-free rats
 - carcinogen- or radiation-induced, absence of tumor viruses, review: 575
- growth rate, host immunity: 945

NEOPLASMS, EXPERIMENTAL (contd.)

- hamster
 - hetero- or homotransplanted, chromosomes: 2664
 - induction, human echoviruses or respiratory syncytial virus: 518
- HeLa cell lines
 - chromosomes: 2630
- high-tumor-producing mouse clone (NCTC-2472)
 - glucose and lactate metabolism: 345, 347
- H-RKB2 (hamster tumor)
 - from peripheral WBC cell line of human infectious mononucleosis: 1709
- immunity, review: 11, 566, 1436, 2141
- Kirsten (mouse) sarcoma virus-induced hamster sarcoma
 - hamster-specific sarcoma virus: 801
- Krebs-2 carcinoma (mouse)
 - DNA, induction of virus-containing mammary tumors, mouse: 419
- L-M cell-induced (mouse)
 - isoaccepting transfer RNA structure: 549
- low-tumor-producing mouse clones (NCTC 2445 or 2555)
 - glucose and lactate metabolism: 345, 347
- melanoma B16 (mouse)
 - effect of anticoagulants: 1469
- methylcholanthrene- or benzpyrene-induced mouse tumors, effect of guinea pig RNA: 1059
- rat tumors, chromosomes: 1053
- MFS8 fibrosarcoma (mouse)
 - cells, stimulation by Krebs cycle metabolites: 615
- Moloney (Gross pseudotype) sarcoma virus-induced hamster tumor
 - hamster-specific sarcoma virus: 802
- mouse
 - formation of metastases, role of RES: 622
 - induced by transformed cells, karyotype: 160
 - surface antigens: 2351
- mouse hepatoma
 - ¹⁹⁸Au liver function test: 169
 - circadian mitotic rhythm: 2617
 - genetic susceptibility, liver and tumor growth kinetics: 2618, 2619, 2620
- MSB-1 tumor (rat)
 - Moloney sarcoma virus rescue, Moloney leukemia virus-infected mouse: 804
- NCTC-2472 fibrosarcoma (mouse)
 - ascites or solid, cell growth kinetics: 1693
- nitrosoguanidine-transformed thymus cells
 - rat fibrosarcoma: 425
- pathogenesis, cell transformation, review: 1006
- polyoma virus-induced (hamster)
 - radiation effects: 855, 856
 - sarcoma, glycoprotein distribution: 862
- polyoma virus-induced (rat)
 - standardization: 311
- RAB-1 sarcoma (mouse)
 - chloroleukemia-inducing virus: 1989
 - Graffi leukemia virus isolation: 813
- radiation effects in vivo, mathematical model: 940

NEOPLASMS, EXPERIMENTAL (contd.)

- rat
 - effect of histidine decarboxylase inhibitors on protein synthesis: 1243
- rat hepatoma
 - cell membrane transport: 976
 - effect of carcinogens: 613, 1151
 - growth kinetics: 140, 1341, 1534, 1694
 - glycolysis: 2262
 - induced or transplanted
 - glucuronyltransferase: 1902
 - glutathionase: 652
 - methylcholanthrene-induced benzpyrene hydroxylase: 1904
 - serum lipoproteins during tumor growth: 1708
 - tumor mitochondria-specific mitochondrial antigen(s): 788, 1435
- Rauscher leukemia virus-induced hamster tumor properties of virus: 1220
- Rous sarcoma virus-exposed baboon
 - effect of dexamethasone: 457
- Rous sarcoma virus-induced hamster tumors
 - clone #9, ultrastructure: 2375
 - properties of long-term cell line: 799
 - reovirus particles: 758
- Sarcoma 37 (mouse)
 - stimulation, hepatoma-susceptibility genotype, mouse: 2620
 - malignancy-associated peripheral WBC changes: 1434
 - virus-like particles, properties: 283
- Sarcoma 180 (mouse)
 - Friend leukemia virus replication: 2342
 - immunosuppression, Friend leukemia virus: 2064
 - malignancy-associated peripheral WBC changes: 1434
- spontaneous
 - chromosomes, rat: 1053
 - hamster carcinoma, properties of DNA: 2648
 - lung, strain differences, mouse: 983, 2643
 - multiple, male hamster, case and review: 2649
- spontaneously-transformed cells
 - ganglioside analysis, mouse: 515
 - mouse, rat or hamster embryo, properties: 977, 979
 - rat lung, pyruvate kinase and lactate dehydrogenase: 553
 - virus particles and collagen content, mouse or rat embryo: 981
- SV40-transformed mouse cells
 - ganglioside analysis: 515
- synchronized mitosis, mathematical model: 942
- T5 tumor (mouse)
 - cell-mediated immunity: 149
- Taper hepatoma (mouse)
 - RNA synthesis: 1427
- transplantable
 - effect of urethan or DNA or RNA, mouse: 621
 - mouse or hamster melanomas, separation of viable tumor cells: 2645
 - rat tumors, effect of Friend leukemia virus, mouse or rat: 2344, 2345

NEOPLASMS, EXPERIMENTAL (contd.)

- sarcoma, effect of immune serum, mouse: 623
 - tumor mitochondria-specific antigen(s), mouse, rat or hamster: 788
 - virus-harboring mouse strains
 - chemotherapy: 1573
 - virus-induced
 - tumor mitochondria-specific antigen(s), animal: 788
 - Walker 256 carcinosarcoma (rat)
 - circadian changes of body temperature, liver catalase and plasma iron: 2652
 - growth kinetics, mathematical model: 2615
 - stimulation, electricity: 1750, 2181
 - Yoshida sarcoma (rat)
 - chromosomes, strain differences: 2665
 - effect of carcinogens: 1146, 1864
 - pyruvate kinase and lactate dehydrogenase: 553
- NEOPLASMS, HUMAN (general and unspecified)
- associated
 - dermatomyositis, cases and review: 1704
 - plantar or palmar keratoses: 2109
 - autoimmunity and virus diseases, review: 1025
 - cellular immunity: 11, 751
 - detection of Epstein-Barr virus particles, method: 828
 - DNA from, lymphoma induction, hamster: 488
 - embryonic, association with congenital malformations, children: 2105
 - epidemiology
 - age-standardized rate calculation, method, aged: 1649
 - Armenian SSR (Chuvash): 2069
 - associations with other diseases, aged men, Australia: 892
 - Brazil (São Paulo), children: 1681
 - Bulgaria, children: 1378
 - California, twins, children: 1680
 - Canada: 894
 - Colombia (Cartagena): 329
 - Congo (Brazzaville): 2514
 - Czechoslovakia (České Budějovice district): 1376
 - Dominican Republic: 1650
 - East Africa: 885
 - Finland: 1380
 - France: 328
 - occupational groups: 2522
 - Germany
 - aged, Magdeburg: 1372
 - diabetes mellitus, Stralsund: 891
 - industrial and non-industrial areas, Hamburg: 1652
 - serum Epstein-Barr virus antibodies, Essen: 2037
 - high-risk diseases, children, review: 2137
 - Hong Kong (Chinese): 1382
 - immunosuppression for kidney transplants: 2087
 - India (Bombay), ethnic groups (Parsis): 2066, 2067
 - international (14 nations): 2513
 - Israel: 530, 879
 - ethnic groups: 1651

EOPLASMS, HUMAN (contd.)

- Italy
 - age factors, Milan: 2096
 - high-mortality rate area (Spoleto): 326
- Jamaica, children: 884
- Kenya (western) and Tanzania (northwestern), geographical variations: 2520
- methods, WHO standards, review: 1445
- migrant populations, international: 1338
- New York and New Jersey, occupational asbestos exposure, review: 2071
- Nigeria (Ilesha township): 2523
- Poland, urban and rural: 2524, 2525
- Rumania: 2515, 2516
- socioeconomic status and smoking: 2070
- solid tumors (neural, angiomatous, teratomatous or embryonal), children, Japan (Nagoya): 1347
- South Africa
 - doctors and dentists, ethnic groups: 1655
 - Johannesburg, ethnic groups: 2068
- South Korea: 944
- Switzerland: 128, 531, 2526
- tropical nations, review: 1448
- U.S.
 - adolescents and children: 890
 - geographical variations, climate, rainfall and soil type: 1342, 1647
 - leprosy: 880
 - newborn infants: 2578
 - smoking, review: 2071
- USSR, urban: 2517
- Washington (Seattle) aged: 893
- familial: 1331
- frequency of constitutional and/or familial chromosome abnormalities: 956, 1003, 1010
- pituitary metastases: 966
- genetics, review: 1436
- growth kinetics
 - host immunity: 945
 - mathematical model: 2613
- infectious mononucleosis induction, Epstein-Barr virus (from Burkitt lymphoma cell line): 1643
- hetero- or homotransplanted, chromosomes: 2664
- immunity, review: 566, 1436, 1446
- lymphocyte blastoid transformation, review: 560
- mesothelioma, identification of asbestos fibers: 412
- multiple endocrine neoplasia syndrome
 - Type 2, pathogenesis, adrenal medullary calcitonin-like factor: 2651
- multiple primary
 - epidemiology
 - Sweden (Malmö): 1664
 - West Virginia: 1354
 - soft tissue sarcoma, breast cancer and other tumors, familial: 914
 - solid tumor(s) with leukemia: 1727, 1811
 - trachea (radiation-cured), esophagus and prostate: 593
 - thyroid cancer: 143
- possible viral etiology, review: 2142
- prevention and competitive risks, review: 1444

NEOPLASMS, HUMAN (contd.)

- psychosomatic aspects: 1411
- risk, appendectomy and/or tonsillectomy, New York (Kings County): 2586
- RNA virus-like particles: 1293
- second primary tumors
 - chronic lymphocytic leukemia: 882
 - risk, breast or female genital cancer, Connecticut: 909
 - thyroid cancer: 143
 - women with salivary gland cancer: 338
- serum
 - glutamic-oxaloacetic transaminase isoenzymes: 344
 - loss of opsonin activity: 1416
- serum antibodies
 - adenovirus-18: 834, 1261
 - associated virus Types 1, 2 and 3, adults and children: 2589
 - T antigens: 2588
 - SV40, children: 1605
- trace metal content: 1135, 1934
- virus superinfection: 869
- NERVOUS SYSTEM NEOPLASMS (See also Brain neoplasms)
 - induction
 - ethylnitrosourea, fetal rat: 635, 637, 1880
 - methylnitrosourea, newborn or fetal rat: 634, 1876
 - rabbit: 253
 - rat: 633
 - phenyldimethyltriazine, rat: 636
 - Turcot's syndrome, associated familial colonic polyposis and Gardner's syndrome: 2654
- NEUROBLASTOMA
 - associated acute cerebellar encephalopathy, cases and review: 2104
 - children, epidemiology, Scotland, U.S. and Canada: 1685
 - familial, child: 2088
 - relationship to von Recklinghausen's disease, child: 2656
- NICKEL
 - analysis, cigarette tobacco and smoke: 686
 - rhabdomyosarcoma of muscle
 - strain difference, rat: 704
 - ultrastructure, rat: 704, 1177, 1178
- NICKEL CARBONYL
 - effect on
 - enzymes, rat liver or lung: 2310
 - RNA, rat liver: 1176
- NICOTINAMIDE
 - metabolites, excretion, smokers: 1484
- NITRATES
 - reduction to nitrosamine (gastric bacteria), human: 639
- NITRITE, SODIUM
 - heart, thymic, kidney or thyroid tumors, rat: 1882
- 5-NITROFURAN DERIVATIVES
 - mammary, kidney, g.i. or ear duct tumors, rat: 417
- NITROGEN MUSTARD (See under Antitumor agents)
- 4-NITROQUINALDINE-N-OXIDE
 - cytotoxicity, effect of adaptation to tobacco smoke, marine plankton: 414

- 2-NITROQUINOLINE
lung tumors, mouse: 251
- 4-NITROQUINOLINE
s.c. sarcoma, mouse: 422
- 4-NITROQUINOLINE 1-OXIDE
chemistry, charge-transfer or free radical reactions: 259, 2277
cytotoxicity, effect of adaptation to tobacco smoke, marine plankton: 414
- 4-NITROQUINOLINE 1-OXIDE
effect on
deoxyribonucleosides, nuclear magnetic resonance spectra: 597
DNA and RNA, mechanism: 227, 230, 1865, 1866, 2276
nucleolus and chromosomes, tumor cells: 1864
proteins and amino acids, mechanism: 228
intestinal, s.c. and lung tumors, rat: 674, 1166
intracerebral implant, induction of obesity, mouse: 620
lung tumors, scar tissue, mouse: 1475
metabolism and distribution, mouse: 432
mutagenesis, bacteriophage: 1862
nitro reduction, rat liver microsomes: 642
osteosarcoma, rat: 2198
reaction with
nicotinamide, mechanism: 1181
phenols: 745
related agents
subeffective doses, mechanism of detection, mouse skin: 229
structure-activity relationship: 1477
skin tumors, effect of nitroquinoline oxide derivatives, mouse: 229
stomach tumors, effect of alkylbenzenesulfonate vehicle, rat: 1476
synthesis: 744
transformed cells, karyotype, hamster embryo cultures: 1863
tritiated, synthesis: 78, 743
uptake, *Tetrahymena pyriformis*: 2275
- 4-NITROQUINOLINE 1-OXIDE, 6-CARBOXY-
transformed cells inducing s.c. tumors, hamster: 2274
- NITROQUINOLINE COMPOUNDS
effect on crustacean eggs: 1861
- NITROSAMINE, N-BUTYL-N-4-BUTANOL-
bladder tumors, rat: 1536
- NITROSAMINE, N-BUTYL-N-ETHYL-
liver or esophagus tumors (benign or malignant), rat: 1535
- NITROSAMINE, COMPOUNDS
alkylnitrosamines, structure-activity relationship: 1867
analysis, spinach: 2278
chromosomal abnormalities, review: 1716
effect on
crustacean eggs: 1861
DNA and RNA, rat liver: 66
environmental, review: 164
enzymatic breakdown, rat liver or kidney: 644
g.i. tumors, DNase and RNase, high- and low-tumor sites, rat: 971
production, gastric bacteria, human: 639, 1529
- NITROSAMINE, DIBUTYL-
bladder tumors, hamster or rat: 244, 1537
respiratory and g.i. tumors, mouse or hamster: 248, 1537
- NITROSAMINE, DIETHYL-
analysis, method, wheat flour: 610
combined with Rauscher mouse leukemia virus, transformation, rat embryo cells: 776
distribution, rat: 1530
effect on
glucuronide metabolism, animal: 1927
glycogen, sex difference, rat liver: 1531
liver regeneration, rat: 204
tissue-specific inhibitor of DNA synthesis, rat liver: 1532
- liver tumors
guinea pig: 191, 654, 655, 656
monkey, serum α -fetoprotein: 62
mouse: 169, 236, 408, 653, 1147, 1547
rat: 193, 194, 195, 196, 399, 400, 416, 1149, 1530, 1534, 1869, 1928
- lung tumors
mouse: 236, 408, 701, 1147, 1547
- lymphoma
leukemia virus activation, mouse: 408
- stomach tumors
mouse: 236, 1147, 1547
- toxicity
liver, fructose phosphate aldolase, rat: 1148
upper respiratory tumors
hamster: 398
- NITROSAMINE, DIMETHYL-
alkylating action of possible metabolite (1,1-dimethylhydrazine), rat tumor: 1146
cytotoxicity, normal or transformed hamster or human cells: 401
effect on liver, trout, frog or bird: 1868
food contamination, South Africa (Transkei): 397
- kidney tumors
fetal mouse: 714
rat: 243, 721, 725, 1145, 2280
- liver tumors
guinea pig: 1533
mouse: 1185, 1870
rat: 192, 247, 721, 1144, 1145
trout: 418
- lung tumors
mouse: 714, 1185, 1870
- toxicity
liver, rat: 1860
monkey or dog: 1871, 2279
- transformed cells
cytotoxicity of nitrosomethylurea or dimethylnitrosamine: 401
reproduction and viability at high temperature: 500
transplacental, effect on embryonic mouse lung, organ culture: 1517
uptake, subcellular fractions, mouse liver: 200
- NITROSAMINE, DIMETHYLTHIO-
toxicity, rat: 247
- N-NITROSOANILINE, N-METHYL-
esophagus tumors, rat: 231

NITROSO COMPOUNDS

liver tumors, mechanism, review: 998
 synthesis from carcinogenic arylhydroxylamines: 738
 teratogenesis, animal: 1859
 transplacental tumor induction
 brain, rat: 1191
 embryonic kidney or lung explants, mouse, review: 2128
 rodent, review: 1005
 upper g.i. tumors, pathology, rat: 638
 -NITROSOGUANIDINE, N-ETHYL-N'-NITRO-
 g.i. tumors, rat or mouse: 1464
 -NITROSOGUANIDINE, N-METHYL-N'-NITRO-
 effect on
 DNA, mechanism, normal or tumor cells: 1151, 1872, 2281
 RNA, rat hepatoma: 1151
 SV40: 2033
 g.i. tumors, rat or mouse: 1464, 1465, 1873, 1874, 1875
 mutagenesis, *Neurospora*: 1158
 transformation, rat thymus cell cultures: 425
 -NITROSOGUANIDINE, N-NITRO-
 chromosome breakage, plant: 1399
 -NITROSO-2-IMIDAZOLIDONE
 mutagenesis, *Saccharomyces*: 742
 -NITROSOMORPHOLINE
 liver tumors, rat: 194, 1884
 ITROSOPIPERAZINE, N,N¹-DI-
 liver and lung tumors, mouse: 1883
 -NITROSOPIPERIDINE
 effect on serum proteins, monkey: 62
 g.i. and lung tumors, mouse: 67
 ITROSO-p-TOLYLSULFONAMIDE, METHYL-
 lung tumors, mouse: 1185
 -NITROSO-2,2,4-TRIMETHYL-1,2-DIHYDROQUINOLINE
 (rubber additive)
 s.c. sarcoma, rat: 39
 -NITROSOUREA, N-ETHYL-
 brain tumors, rat: 1881
 dysontogenic skin tumors, fetal pig: 249
 effect on spontaneous tumor incidence, line A mice: 2282
 mammary and female genital tumors, pregnant rat: 713, 723
 transplacental tumor induction
 brain or nerves, rat: 635, 637, 1880, 2283
 lung, mouse: 1152
 -NITROSOUREA, N-METHYL-
 brain tumors
 dog: 1153
 rabbit: 242, 253, 254, 1519, 1877, 1878
 rat: 37, 631, 632, 633, 634, 1876, 1877, 1880, 1881, 2269, 2270, 2283, 2284
 cytotoxicity, normal or transformed hamster and human cells: 401
 effect on
 fetal brain, rat: 1876, 1879
 nucleic acids, normal cells or cell-free system: 1150, 1518
 intestinal adenocarcinoma, hamster: 1154
 kidney tumors, fetal mouse: 714
 lung tumors, mouse: 714, 1185
 rat: 37
 lymphoma, mouse: 402, 1185, 1935

N-NITROSOUREA, N-METHYL (contd.)

mammary or genital tumors, pregnant rat: 713
 mechanism of action, bacteria and tumor cells: 1155
 soft tissue tumors, dog: 1153
 toxicity, thymus, lymph nodes and bone marrow, mouse: 1557
 transplacental
 effect on
 embryonic mouse lung culture: 1517
 spontaneous leukemia incidence, AKR mice: 2282
 tumor induction, rat or mouse: 634, 714, 1876
 N-NITROSOUREA, N-METHYL-, 2-DEOXY-D-GLUCOSE
 DERIVATIVE (streptozotocin)
 mechanism of action, bacteria and tumor cells: 1155
 NITROSOUREA COMPOUNDS
 mutagenesis, structure-activity relationship: 741
 N-NITROSOURETHAN, N-METHYL-
 effect on DNA, cell-free system: 1150
 lung tumors, mouse: 1185
 mechanism of action, bacteria and tumor cells: 1155
 NOISE (See under Stress)
 19-NORPROGESTERONE, 17 α -HYDROXY-
 effect on methylcholanthrene uterine tumors, mouse: 1901
 NUCLEASES
 distribution
 cancer-susceptible sites, human or rat g.i. tract: 971, 1424
 Friend leukemia virus-infected mouse spleen: 765, 1306
 NUCLEIC ACIDS, DNA
 adenovirus
 infected, transformed or tumor cells: 514, 835, 836, 837, 838, 1263, 1320, 2059, 2145, 2400, 2512
 Agrobacterium tumefaciens phage, plant tumors: 2500
 avian myeloblastosis virus
 infected or tumor cells: 465, 780, 2378
 effect of
 amino acids, fish melanoma explants: 334
 carcinogens
 bacteria: 364, 616, 2239
 bacteriophage: 1168, 1490
 cell-free system: 667, 1112, 1174, 2276
 in vivo, rat or mouse: 46, 66, 204, 367, 621, 630, 1069, 1204, 1518, 1523, 1524, 1564, 1845, 1851, 1853, 1855, 1868, 1870, 1872, 1892, 1893, 1921, 2235, 2244, 2245, 2246, 2253, 2256
 mechanism: 227, 387, 567, 1011, 1088, 1150, 1151, 1155, 1919, 1920, 1937, 2203, 2206, 2233
 normal cells: 36, 230, 232, 619, 1801, 2281
 tumor cells: 621, 1106, 1805, 1865, 1866
 contraceptive hormones, human cervix: 1425
 epithelial growth factor, mouse mammary tumors in vitro: 139

NUCLEIC ACIDS, DNA (contd.)

hypophysectomy, rat hepatoma: 1534
 isoproterenol, rat salivary gland: 1930
 luteoskyrin, tumor cells: 1172
 Epstein-Barr virus
 properties: 831, 1257, 2034, 2035
 euchromatin or heterochromatin, normal or
 leukemic human WBC: 982
 Friend or Moloney leukemia virus-infected cells:
 806, 1306, 1571
 frog virus 3-infected cells: 2498
 Hodgkin's disease lymph node, induction of
 virus formation, HeLa cells: 1294
 hormone effects, virus-induced hyperplastic
 alveolar mammary nodules, mouse: 292
 isolation (animal or human tumors) and tumor-
 inducing effects: 419, 488
 malignant transformation, review: 1450
 mammalian, toxicity, amphibian: 628
 mammary tumor virus-infected mouse cells: 2394
 Marek's disease virus
 comparison to cytomegalovirus DNA: 511
 infected duck embryo cells: 2488
 Moloney or Harvey sarcoma virus
 infected, transformed or tumor cells: 803,
 806, 1590, 1956, 1958
 pathogenesis of human leukemia and lymphoma,
 review: 1458
 polyoma virus
 infected, transformed or tumor cells: 10,
 117, 492, 493, 494, 861, 1608, 2012,
 2144, 2463, 2464, 2465, 2467, 2469
 properties
 exptl. tumors: 37, 140, 197, 632, 1054,
 1080, 2228, 2648
 human tumors: 922, 923, 938, 1420, 1426,
 2614
 radiation-induced leukemia or thymoma, mouse:
 29, 2164
 Rous sarcoma virus
 infected, transformed or tumor cells: 276,
 455, 456, 465, 780, 795, 1245, 1941,
 2386, 2388, 2648
 Shope fibroma virus
 infected rabbit cells, effect of contact
 inhibition or radiation: 2475
 isolation and properties: 1610
 Shope papilloma virus
 rabbit tumors: 2473
 skin, mouse with methylcholanthrene lymphoma:
 225
 spermatic, possible induction of cervix cancer:
 706
 SV40
 infected or transformed cells: 10, 501,
 851, 1280, 1289, 1316, 2025, 2400, 2434,
 2435, 2437, 2439, 2446, 2447, 2451, 2506
 tissue-specific inhibitor from liver, effect
 of carcinogens, rat: 1532
 viral carcinogenesis, mechanism, review: 577
 "virus-free" Burkitt lymphoma cell line: 2479
 Yaba poxvirus-infected monkey kidney cells:
 2477
 NUCLEIC ACIDS, RNA
 adenovirus
 infected, transformed or tumor cells: 514,
 835, 839, 1260, 2145, 2424

NUCLEIC ACIDS, RNA (contd.)

avian myeloblastosis virus-infected or
 leukemic cells: 1230, 1995, 2054, 2377, 2378
 bacteriophage, effect on adenovirus-12 tumor
 induction, hamster: 840
 Burkitt lymphoma cells: 2029
 carcinogen-induced tumors, rat or mouse:
 225, 396, 1143, 1144, 1173, 2228, 2258
 effect of
 antitumor antibiotic, avian viral leukemic
 WBC: 1577
 carcinogens
 bacteria: 1155, 2250, 2252
 cell-free system: 1112, 1174, 1184
 in vivo, rat or mouse: 66, 201, 380,
 621, 1157, 1176, 1208, 1518, 1524,
 1535, 1538, 1564, 1851, 1853, 1855,
 1868, 1893, 1920, 1921, 1937, 2235,
 2243, 2244, 2245, 2253, 2255
 mechanism: 387, 567
 normal cells: 230, 232, 1471, 1828
 tumor cells: 621, 1106, 1146, 1151, 1805
 contraceptive hormones, human cervix: 1425
 frog virus 3-infected human tumor cells: 2498
 GA (Marek's disease-associated) virus-induced
 liver tumor, chick: 1319
 guinea pig tissues, effect on benzpyrene- or
 methylcholanthrene-induced mouse sarcomas:
 1059
 isoaccepting transfer RNA, L-M cell cultures
 and L-M cell-induced mouse tumors: 549
 mammalian, toxicity, amphibian: 628
 metabolism, breast cancer or fibrocystic
 disease: 938
 mouse leukemia-sarcoma virus complex
 infected, transformed or tumor cells: 450,
 803, 806, 1246, 1306, 1571, 1583, 1590,
 1944, 2335
 mouse mammary tumor virus
 isolation and properties: 2001
 normal or malignant human cells: 950, 1968,
 1970
 pathogenesis of human leukemia and lymphoma,
 review: 1438
 polyoma virus-infected cells: 495
 Rous sarcoma virus
 infected, transformed or tumor cells: 276,
 454, 455, 784, 795, 1583, 1944, 2371,
 2386, 2388
 SV40
 infected, transformed or tumor cells: 501,
 1283, 1316, 2029, 2030, 2424, 2451
 synthesis, normal or neoplastic mouse liver:
 1427
 transfer RNA-methylating enzymes, mouse or rat
 mammary tumors: 2647
 viral carcinogenesis, mechanism, review: 8,
 577
 NUCLEIC ACIDS, RNA, SYNTHETIC POLYMER
 (polyinosinic-polycytidylic acid)
 autoimmunity induction, NZB/NZW mouse: 444
 effect on
 adenovirus-12 tumor induction, hamster:
 840
 effect on
 dimethylbenzanthracene skin tumors, mouse:
 378

UCLEIC ACIDS, RNA, SYNTHETIC POLYMER (contd.)

- Friend virus leukemia or sarcoma, mouse: 841, 1303
- methylcholanthrene-induced transplanted tumors, mouse: 1516
- Moloney or virus-induced sarcoma, mouse: 461, 1303
- mouse sarcoma or leukemia viruses in vitro: 451, 843
- Rous sarcoma or Marek's disease virus infection, chicks: 512
- SV40 tumor induction, hamster: 842

UCLEIC ACIDS, RNA, SYNTHETIC POLYNUCLEOTIDE

- effect on viral carcinogenesis, review: 2140

UCLEOHISTONES

- properties, adenovirus-12 or adenovirus-2/SV40 hamster tumors: 486

UCLEOLUS

- abnormalities, lead salt-induced kidney or lung tumors, frog: 2309
- effect of nitroquinoline oxide, tumor cells: 1864
- morphology, transitional cell carcinoma of bladder or renal pelvis: 2660
- SV40-infected human embryo cells: 2020

UCLEOPROTEINS

- effect of methylcholanthrene, rat liver: 2325
- ribonucleoprotein
- effect on limb regeneration, frog: 984
- Rous sarcoma virus A and C particles, transformed cells: 787

UCLEOSIDES AND NUCLEOTIDES

- deoxythymidine and other deoxyribonucleosides, effect of nitroquinoline oxide, nuclear magnetic resonance spectra: 597
- oligonucleotides, effect of fluorenylacetamide: 1929
- polynucleotides, effect of aflatoxin, cell-free system: 1112
- ribonucleotide reductase, Yaba virus-induced monkey tumors: 125
- specific metabolic abnormalities, ethionine- or α -naphthylisothiocyanate-induced hepatoma, rat: 1173
- thymidine triphosphate, metabolism, methyl-dimethylaminoazobenzene liver tumors, rat: 1142

UCLEUS

- ultrastructure, adenovirus 5-infected human tumor cells: 2404

OCCUPATIONAL DISEASES

- acetone and phenol production
- carcinogenic effects (animals) of intermediate pyrolytic resins: 2304
- aflatoxin exposure
- possible toxic dermatosis: 669
- arsenic exposure
- chronic toxic symptoms, Poland (Zloty Stok): 1118
- respiratory cancer, possible effect of sulfur dioxide air pollution: 1699
- U.S.: 926
- asbestos exposure
- asbestos needles in lungs: 680

OCCUPATIONAL DISEASES (contd.)

- bronchial cancer: 1762
- cancer incidence, New York and New Jersey, review: 2071
- leukemia/lymphoma, New York: 1763
- mesothelioma: 681, 1482
- West Germany (Hamburg): 1370
- benzene exposure
- chromosomal abnormalities, age factors: 952
- erythroleukemia, chromosomes: 951
- benzene or toluene derivatives
- leukemia: 369, 370, 371, 372
- bladder cancer: 690, 920, 929, 1782
- β -naphthylamine or benzidine exposure, U.S.: 545
- rubber manufacturing, Britain: 544, 606, 927, 1119
- toxicity of polymerized rubber additive, rat: 606
- cancer and heart disease risk
- France: 2522
- cancer epidemiology
- anesthesiologists, U.S. and Canada: 888
- chemists, U.S.: 933
- doctors and dentists, South Africa, smoking: 1655
- industrial areas of West German city (Hamburg): 1652
- chemical or radiation carcinogenesis, review: 6
- dust exposure
- chronic bronchitis, smoking, coal miners, Germany: 1117
- lung cancer, smoking, coal miners, Scotland: 1659
- nasal cavity and sinus tumors, shoe manufacturing or bakery workers, England (Northamptonshire): 1658
- pneumoconiosis with/without asbestosis, lung cancer, Japan: 2320, 2321
- environmental carcinogen exposure
- larynx cancer, Czechoslovakia: 881
- lung or esophagus cancer, South Africa, ethnic groups: 928
- esophagus cancer
- Africa (high- or low-incidence nations) and U.S. (nonwhite): 1698
- heavy metal exposure
- cancer risk, review: 996
- larynx cancer
- farmers and other groups, Ukrainian SSR: 2534
- mineral oil exposure
- cancer of scrotum: 1767
- occupational status, cervix or uterus cancer, Poland: 520
- radiation exposure
- leukemia, Japan: 2166, 2167
- lymphoma or lung cancer: 1755
- skin, bone or soft tissue tumors: 1452
- WBC chromosomes: 1030
- silicosis
- primary hemangioendothelial tumor of heart: 682
- sinapylaldehyde exposure
- nasopharynx cancer, review: 1004

OCCUPATIONAL DISEASES (contd.)

- skin cancer
 - epidemiology, Britain: 889
 - medicolegal review: 1717
- solid fuel exposure
 - lung cancer, international: 179
- stomach cancer
 - mining region of Utah: 2552
 - pesticide exposure, case and review: 1720
- tobacco processing
 - respiratory diseases, Poland: 172
- toxoplasmosis
 - farmers, brain tumors, Minnesota: 2579
- wood exposure
 - ethmoid and paranasal sinus tumors: 368
- 2,6-OCTADIENAL, 3,7-DIMETHYL- (citral)
 - effect on benzpyrene-induced squamous metaplasia, hamster trachea in vitro: 1795
- OILS, EDIBLE
 - crude corn oil
 - stomach tumors, mouse: 2328
 - heated, s.c. or g.i. tumors, rat: 241
 - margarine or chocolate
 - carcinogen content, processing methods, Germany: 604
 - sunflower oil
 - effect on fluorenylacetylamide carcinogenesis, rat: 1842
- OIL, ESSENTIAL
 - citrus, effect on dibenzpyrene s.c. tumors, mouse: 1214
- OIL, MINERAL (See also Petroleum and petroleum products)
 - hepatoma, rat: 430
 - occupational exposure, cancer of scrotum: 1767
- OIL, MINERAL (See also Petroleum)
 - plasmacytoma
 - germ-free or conventional mice: 1175
 - leukemia virus-like particles, mouse: 1250, 1251, 1298
 - mammary tumor virus-like particles, mouse: 730
 - transplantable tumors, pathology, mouse: 406, 1492
- OOPHORECTOMY (See under Endocrine ablation)
- ORCHIECTOMY (See under Endocrine ablation)
- OROPHARYNX NEOPLASMS
 - epidemiology
 - U.S., environmental factors and ethnic groups: 1384
- OROTIC ACID
 - effect on liver carcinogenesis, rat: 1847
- OVARY
 - gonadotropin response, effect of dimethylbenzanthracene, mouse or rat: 216
 - persistent stromal theca cells, postmenopausal women with endometrial cancer: 548
- OVARY NEOPLASMS
 - epidemiology
 - New York (upstate): 2577
 - relationship to leukemia, Japan: 2601
 - familial
 - dysgerminoma, adolescent sisters: 2659
 - mother and daughters: 886
 - genetically susceptible mouse strain, hair loss patterns: 2268

OVARY NEOPLASMS (contd.)

- homology to tumors of testis: 1383
- human, isolation of chick sarcoma-inducing virus from serum or tumor: 1645
- induction
 - dimethylbenzanthracene, mouse: 210, 217, 218, 649, 1074, 1522
 - lead acetate, rat: 1131
 - methylcholanthrene, rabbit: 1047
 - ovarian autograft, rat: 1832
- malignant or preinvasive, karyotype: 342
- radiation-induced, mouse: 1754, 2178
- second primary tumor, risk, breast cancer, Connecticut: 909
- sex cord tumor, familial polyposis of colon (Peutz-Jeghers syndrome): 1403
- teratoma, spontaneous, mouse leukemia virus-containing, mouse: 1231
- 6H-1,2,4-OXADIAZINE, 5-ACETAMIDO-3-(5-NITRO-2-FURYL)-
 - hemangioendothelial sarcoma and mammary tumors, rat: 426
- OXALACETIC ACID
 - stimulation of tumor cells in vitro: 615
- OZOKERITE (See under Wax, medicinal)
- PANCREAS
 - exocrine, effect of fluorenylacetylamide, ultrastructure, rat: 64
- PANCREAS NEOPLASMS
 - epidemiology
 - chemists, U.S.: 933
 - Germany (Heidelberg), chronic pancreatic diseases: 521
 - Massachusetts, diabetes mellitus: 2519
 - Scotland (northeastern), diabetes mellitus: 1666
 - induction, oral contraceptive, rat: 1830
- PARASITES
 - Cysticercus, effect on dimethylaminoazobenzene hepatoma, rat: 198
 - infection, liver tumors, international: 2561
 - Trichosomoides crassicauda, bladder infestation, effect on fluorenylacetylamide bladder tumors, rat: 1171
- PARATHYROID
 - hyperplasia, incidence, strain differences, rat: 1433
- PENIS NEOPLASMS
 - syphilis lesion: 1401
- PERITONEAL NEOPLASMS
 - induction, plastics, rat: 1132
 - mesothelioma, occupational asbestos exposure: 681
- PERYLENE
 - analysis, medicinal wax (ozokerite ceresin) from USSR: 2307
 - biosynthesis, bacteria, effect of culture medium constituents: 1093
 - metabolism, mouse embryo cells: 2219
 - skin tumors, mouse: 1784
- PESTICIDE SYNERGISTS
 - effect on benzpyrene metabolism, rat: 1095
- PESTICIDES (See also Herbicides and Insecticides)
 - liver and other tumors, mouse: 31

- ESTICIDES (contd.)
 occupational exposure, cancer risk, case and review: 1720
- ETROLEUM AND PETROLEUM PRODUCTS (See also Air pollution, Engine exhaust gases and Oil, mineral)
 additives of medicinal wax (ozokerite ceresin) from USSR, carcinogen content: 2307
 automobile exhaust, air pollution, USSR (rural): 735
 diesel oil
 benzpyrene-containing, yeast culture, hydrocarbon synthesis: 2207
 combustion products, salt-drying method, benzpyrene content: 2210
 fuel consumption, air pollution, cancer epidemiology, France: 2521
 gas combustion products, effect on benzpyrene content of fish: 2208
 gasoline, quality, effect on benzpyrene in exhaust, Soviet automobiles: 1481
 petrochemical effluents, benzantracene content, analytical method: 1827
 processing, air pollution, bioassay method: 1791
 refining products, benzpyrene content: 2211, 2213
 soil contamination
 bioassay method (mouse skin): 2213
 refinery or airport area, USSR: 1086, 2212
- IARYNGOESOPHAGEAL DIVERTICULUM
 malignant transformation, cases: 2670
- IARYNX NEOPLASMS
 epidemiology
 India (Madhya Pradesh), ethnic groups, tobacco chewing: 2531
 Natal (Durban), ethnic groups, betel chewing: 1656
 Poland (Cracow): 528
 smoking and dietary factors, Puerto Rico: 932
- INACETIN
 abuse, bladder or kidney cancer, Sweden: 1123, 2545
- INANTHRENE
 metabolism, effect of methylcholanthrene, rat liver microsomes: 1049
- INANTHRENE, 3-ACETAMINO-
 leukemia, rat: 246
- INANTHRENE, AMINO-, DERIVATIVES
 mammary tumors, rat: 246
- INANTHRENE, N-HYDROXY-2-ACETYLAMINO-, ACETIC ACID ESTER
 mutagenesis, bacteria: 2239
- INANTHRENE 9,10-OXIDE
 metabolism, rat liver enzyme: 379
- INANTHRENE DERIVATIVES
 cysteine conjugates, effect on aminoacyl-RNA synthetase, cell-free system: 1184
- INANTHRO(2,1- α)THIAZOLE
 skin tumors, mouse: 1470
- INANTHRO(2,1- α)THIAZOLE, 2-METHYL-
 skin tumors, mouse: 1470
- 2-PHENANTHRYLACETAMIDE, N-ACETOXY-
 synthesis: 2238
- ENIDONE (See 3-Pyrazolidinone, 1-phenyl-)
- PHENOBARBITAL
 effect on diethylnitrosamine carcinogenesis, mouse: 236
- PHENOL COMPOUNDS
 cocarcinogenic, excretion, germ-free or conventional rats: 1489
 production, intermediate pyrolytic resins, skin tumors and leukemia, animal: 2304
- PHENYLBUTAZONE
 acute leukemia, genetic factors, human: 1911
 toxicity, rat: 1922
- PHORBOL ESTERS (See Croton oil phorbol esters)
- PHOSPHOLIPIDS
 effect on methylcholanthrene tumors, mouse: 1064
 liver
 dimethylaminoazobenzene hepatoma, effect of riboflavin or antitumor antibiotic, rat: 1139
 effect of hepatocarcinogen, rat: 1886
- PHOTOGRAPHIC FILM
 emulsion component or developing agent, toxicity, rat or mouse: 2305
- PHTHALATE DERIVATIVES
 mutagenesis and effect on tumor incidence, Drosophila: 626
- PITUITARY
 graft, mammary tumors, rat: 1504
- PITUITARY NEOPLASMS
 estrone-induced or spontaneous, plasma prolactin levels, rat: 728
 induction
 estradiol, mouse or rat: 1129, 1501
 lead acetate, rat: 1131
 oral contraceptive, rat: 1830
 mammatropic or mammosomatotropic, Type C virus particles, rat: 2000
 metastatic, frequency, breast and other cancer: 966
 prolactin-producing, radioimmunoassay of hormone, rat: 727
- PITUITARY-ADRENAL SYSTEM
 hormonal carcinogenesis, review: 2120
 stimulation by stress, effect on methyl-dimethylaminoazobenzene liver tumors, rat: 2179, 2180
- PLANARIA
 methylcholanthrene, benzpyrene or benzantracene tumors: 627
- PLANT NEOPLASMS
 induction, Agrobacterium tumefaciens phage DNA: 2500
- PLANT PREPARATIONS
 legumes, mitogenic properties, normal human lymphocytes: 33
 taenicides, liver cancer, Ethiopia: 2084
- PLANTS
 benzpyrene content, soil of low or high benzpyrene level: 1086, 1787, 1792, 2212
- PLASMACYTOMA (See under Myeloma and related diseases)
- Plasmodium berghei yoelii
 infection, effect on Harvey viral sarcoma, mouse: 1960
- PLASTICS (See also Polymers)
 polyethylene
 containers, contamination of asbestos samples: 32

PLASTICS (contd.)

- s.c. sarcoma, rat: 38
- pre malignant cervical, uterine and vaginal lesions, mouse: 1836
- s.c. tumors
 - mouse: 2300
 - rat: 1132, 1543, 2117
 - radiation effects, rat or dog: 2299

PLEURA NEOPLASMS

- mesothelioma
 - asbestos detection, method: 181
 - induction, rat: 183, 1101
 - cultures, comparison with normal mesothelial cells: 1418
 - occupational asbestos exposure: 681, 1482
 - West Germany (Hamburg): 1370

POLYANIONS

- effect on avian sarcoma viruses: 782

POLYCATIONS

- effect on avian sarcoma viruses: 782

POLYCYTHEMIA VERA

- treated or untreated, chromosomes: 2641

POLYINOSINIC-POLYCYTIDYLIC ACID (See Nucleic acids, RNA, synthetic polymer)

POLYMERS

- basic, induction of specific viral repressor, abortively or productively SV40-infected cells: 853
- cholesterol or glycerol, s.c. sarcoma, rat: 1544
- methyl 2-cyanoacrylates (surgical adhesives), s.c. tumors, mouse: 2306

POLYOMA VIRUS (See under Virus, papova)

POLYVINYLPYRIDINE N-OXIDE

- leukemia and mammary tumors, mouse or rat: 717

PONCEAU MX (food coloring)

- liver toxicity, mouse: 609

PREGNANCY

- cervix cancer
 - Oklahoma (Oklahoma City): 906
 - Pennsylvania (Philadelphia): 907
- effect on
 - dimethylbenzanthracene mammary carcinogenesis, rat: 57
 - genital and mammary tumor induction, alkyl-nitrosoureas, rat: 713, 723
 - normal or pathological, host immunity and hormonal feedback mechanism, human and animal: 967
 - placental aryl hydrocarbon hydroxylase activity, smoking, human: 685
 - prenatal radiation exposure, cancer latent periods, children: 2169
 - reproductive histories
 - breast cancer, Greece (Athens): 2079
 - international: 2565
 - Japan (Tokyo): 2566
 - Massachusetts (Boston): 1356
 - Taiwan: 2567
 - Wales (southern): 1385
 - cervix cancer, U.S.: 2568
 - leukemia risk, France: 2594
 - ruptured placental membranes, benzpyrene diagnosis, human: 1798
 - transplacental carcinogenesis
 - adenovirus-12, hamster: 1262

PREGNANCY (contd.)

- benzpyrene, lung, mouse: 2329
- cat fibrosarcoma virus, kittens or puppies: 2392
- dimethylbenzanthracene, skin, mouse: 2329
- embryonic kidney or lung cultures, mouse or rat: 714, 2128, 2224
- ethylnitrosourea, brain, rat: 635, 637, 2283
- lung, mouse: 1152
- rat: 1880
- swine: 249
- mechanism, review: 2116
- methylnitrosourea, leukemia incidence, AKR mice: 2282
- rat: 634, 1876
- mouse leukemia viruses: 2352
- nitroso compounds, brain, rat: 1191
- rodent, review: 1005
- Shope papilloma virus, skin, rat: 1327
- tubal-ligation sterilization, cervix cancer epidemiology, Puerto Rico: 2574
- PROCARBAZINE (See under Antitumor agents)
- PRODIGIOSAN (See under Antitumor agents)
- PROGESTERONE
 - effect on
 - dimethylbenzanthracene tumors, rat or mouse: 1128, 1824
 - transplantable mammary tumors, mouse: 2267
- β -PROPIOLACTONE
 - effect on bacteria and bacteriophage: 1490
 - skin tumors, mechanism, mouse: 1921
- PROPIOPHENONE, p-HYDROXY-
 - effect on dimethylaminoazobenzene liver tumors, mouse: 1467
- PROSTATE
 - methylcholanthrene-transformed cell lines, mouse: 226, 388, 1065, 2185
 - spontaneously transformed cell lines, mouse, properties: 348
- PROSTATE NEOPLASMS
 - epidemiology
 - India (Bombay), ethnic groups: 2066
 - Japan, relationship to leukemia: 2601
 - Oklahoma, ethnic groups: 1353
 - human, herpesvirus-like particles: 2044
 - induction
 - lead acetate, rat: 1131
 - methylcholanthrene, rat: 390, 1052
 - SV40, hormone sensitivity, hamster: 506
 - testosterone + methylcholanthrene, mouse: 716
 - viral etiology, review: 576
- PROTEIN SYNTHESIS
 - avian myeloblastosis virus-infected blood cells, chick: 2377
 - effect of
 - carcinogens
 - bacteria: 1155
 - normal cells: 1192, 1564, 1828
 - tumor cells: 1106, 1155
 - contraceptive hormones, human cervix: 1425
 - histidine decarboxylase inhibitors, rat tumors: 1243
 - myeloma proteins, mouse myeloma cultures: 1428
 - polyribosomes, effect of tannic acid, rat liver: 1179

- ROTEIN SYNTHESIS (contd.)
 relationship to growth kinetics, mouse tumor: 1701
 Rous sarcoma virus-infected cells: 454
 SV40-infected cells: 1286
- ROTEINS
 albumin, effect on benzpyrene hydroxylase, rat liver microsomes: 1091
 analysis, carcinogen-induced rat tumors: 37, 193, 194, 651, 1848
 carcinogen binding, mouse or rat tissues: 47, 228, 698, 1524, 1540, 1777, 1805, 1851, 1852, 1853, 1854, 1885, 1890, 1891, 1921, 2221, 2242
 cytoplasmic, nitroquinoline oxide uptake, *Tetrahymena pyriformis*: 2275
 dietary deficiency, liver cirrhosis and hepatoma, rat: 673
 liver
 effect of carcinogens, rat or mouse: 1060, 1061, 1062, 2234
 dimethylnitrosamine, trout, frog or bird: 1868
 Rous sarcoma virus-infected cells with/without nuclear fragmentation: 795
 serum α_1 -fetoprotein
 dietary pyridoxine deficiency, primate: 970
 induced hepatoma, monkey: 62
 SV40 capsid, analysis: 2031
 tyrosine-containing, adenovirus-12-transformed hamster embryo cells: 839
- ROTOZOA
 ameba, effect of aflatoxin: 1916
Tetrahymena pyriformis
 effect of tobacco smoke on mitochondria: 1483
 nitroquinoline oxide uptake: 2275
- SYCHOKINESIS
 effect on exptl. tumors: 985
- PSYCHOLOGICAL FACTORS
 effect on animal tumors, review: 1711
 psychosomatic aspects of cancer: 1411, 1412
- Teris aquilina* (bracken fern)
 g.i. and bladder tumors, rat or mouse: 68, 1781, 2314
- URINE N-OXIDES
 s.c. tumors, structure-activity relationship, rat: 1189
- PYRAZOLIDINONE, 1-PHENYL-
 toxicity, rat or mouse: 2305
- URENE
 metabolism
 effect of methylcholanthrene, rat liver microsomes: 1049
 mouse embryo cells: 2219
- URIDOXINE
 dietary deficiency
 liver cancer epidemiology, Africa: 970
 serum α_1 -fetoprotein, primate: 970
 effect on tryptophan metabolism, smokers: 1099
- URROLIZIDINE ALKALOIDS
 liver toxicity, rat: 2308
- QUINAZOLINE, 2-METHYLTRICYCLO-
 effect on skin histochemistry, mouse: 2271
- QUINAZOLINE, 3-METHYLTRICYCLO-
 skin tumors, mouse: 2271
- QUINAZOLINE, TRICYCLO-
 epidermal hyperplasia, mouse skin: 1188
- QUINOLINE, 4-AMINO-, 1-OXIDE
 effect on DNA and RNA, normal cells: 230
- QUINOLINE, 0,0'-DIACETYL-4-HYDROXYAMINO-, 1-OXIDE
 free radical formation and mechanism of action: 1165
- QUINOLINE, 4-HYDROXYAMINO-
 DNA inactivation, mechanism, bacteria: 616
- QUINOLINE, 4-HYDROXYAMINO-, 1-OXIDE
 effect on DNA and RNA, normal or tumor cells: 230, 1865
 intracerebral, induction of obesity, mouse: 620
 stomach and other tumors, rat: 428
 transformation, chromosomes, hamster embryo cells: 1863
- QUINOLINE, N-NITROSO-2,4-TRIMETHYL-1,2-DIHYDRO-, POLYMERIZED (rubber additive)
 s.c. tumors, rat: 606
- QUINOLINE COMPOUNDS
 DNA photosensitization: 2203
- QUINOLINIC ACID
 excretion, dietary factors, Africa (Uganda): 1368
- RADIATION CARCINOGENESIS, EXPERIMENTAL
 bone, rabbit: 1028
 cell growth kinetics, review: 2125, 2126, 2127
 cervix uteri, mouse: 1036
 connective tissue, rabbit: 1028
 dose-response curve, mouse: 1754
Drosophila: 27
 effect of altitude, mouse: 1749
 endocrine tumors, rat: 2177
 γ -irradiation, effect of UV, mouse: 1744
 lung
 mouse: 1039, 2178
 rat: 2171, 2176
 mammary, rat: 1746
 mathematical models: 22
 mouse: 1758
 ovary, liver and RES, mouse: 2178
 skin
 mouse: 168, 2124
 rabbit: 1028
 rat: 1038
 thyroid, rat: 2175, 2257, 2265
 review: 2132
⁹⁰Sr, bone, swine: 26
 stomach, mouse: 167
 uterus or Harderian gland, effect of diet, mouse: 1461
- RADIATION CARCINOGENESIS, HUMAN
 bone
 child with retinoblastoma: 588
 Hiroshima and Nagasaki: 1027
 or soft tissue, occupational or therapeutic radiation exposure: 1452
 breast, postpartum mastitis radiotherapy, New York (upstate): 23
 cervix: 1737
 children, prenatal irradiation, latent periods: 2169

RADIATION CARCINOGENESIS, HUMAN (contd.)

- corpus uteri, possible: 1037
- maxillary carcinoma, basal cell nevus syndrome (familial): 2163
- mechanism, review: 2131
- occupational
 - lung cancer incidence: 1755
 - review: 6
- radiotherapy of tracheal cancer, second (esophagus) and third (prostate) primary tumors: 593
- reticulum cell sarcoma, cancer radiotherapy-induced, cases: 1745
- skin: 1452, 1740, 1743
 - head and neck: 25
- sunlight
 - lip cancer, U.S., geographical variations: 2530
 - melanoma, Australia: 558, 1381
 - or radiotherapy, lupus vulgaris with malignant transformation: 595
 - skin cancer
 - albinism, Nigeria: 1667
 - pathogenesis: 2161
 - Sweden: 2529
- therapeutic pneumothorax with fluoroscopy (for TB), risk of breast or lung cancer: 1042, 1748
- thorium, bile duct carcinoma: 2170, 2172
- thyroid: 30
 - epidemiology
 - Japan (Hiroshima/Nagasaki): 930
 - New York (Rochester): 2173
 - risk, irradiated cold nodules of thyroid: 1705

RADIATION EFFECTS

- adenovirus-31 transformation efficiency, hamster embryo cells: 846
- bone marrow chromosomes
 - atomic radiation-exposed subjects, Hiroshima: 591, 1757
 - rat: 590
- cellular RNA synthesis, Shope virus-infected rabbit cells: 2475
- chromosome breakage, plant: 1399
- dimethylbenzanthracene mammary tumors, rat: 1041
- exptl. tumors in vivo, mathematical model: 940
- fluorenylenebisacetamide liver tumors, rat: 1508
- fowl plague virus multiplication, singly- or doubly-infected cells: 780
- Friend virus leukemia, mouse: 99
- goitrogenic capacity of thyroid, rat: 2174
- host immunity, methylcholanthrene-induced sarcoma, mouse: 2196
- infectivity and tumorigenicity (hamster) of simian adenovirus SA-7: 1315
- laser, effect on DMBA-induced dyskeratosis, hamster cheek pouch: 1926
- leukemia incidence and kidney diseases, RF/Uln mouse strain: 1040
- liver cancer incidence, Japan (Hiroshima/Nagasaki): 2559
- mammary tumor virus activation, 020 strain mice: 818

RADIATION EFFECTS (contd.)

- mouse cell cultures, sarcoma-forming effect and virus induction: 1752
- occupational exposure, WBC chromosomes: 1030
- plastic implant tumor development, rat or dog: 2299
- polyoma virus, cell cultures or hamster: 496, 855, 856, 2010, 2014
- postponement of radiation leukemogenesis, mouse: 21
- promotion of viral leukemia, rat: 20
- Rous virus chick embryo cells: 2381, 2387
- short-wave irradiation of brain, effect on methylcholanthrene tumors, rat: 2192
- skin carcinogenesis by detergent additives, mouse: 2301
- stimulation of brain tumor, human: 1747
- sunlight, seasonal leukemia incidence, Poland (Cracow): 1392
- surface antigens, EB virus-positive Burkitt lymphoma cell lines: 1617
- SV40, cell cultures or hamsters: 846, 857, 1288, 1751
- thyroid tumor promotion, human: 1029
- transformed hamster embryo cells, reproduction and viability at high temperature: 500
- transplanted mammary tumor, mouse: 28
- tumor growth, high- or low-tumor-producing cell clones, mouse: 347
- urethan lung carcinogenesis, mouse: 1081, 1841
- UV effect on γ -radiation tumorigenesis, mouse: 1744
- virus-free preneoplastic mammary outgrowths, mouse: 1836
- Yaba monkey poxvirus: 868

RADIATION LEUKEMOGENESIS, EXPERIMENTAL

- cell growth kinetics, thymus: 2164
- dog, ^{90}Sr : 1034
- effect of
 - Gross leukemia virus, rat: 2355
 - mouse: 29, 361, 589, 1033, 1035, 1228, 1454, 1461, 1749, 1754, 2178, 2351, 2355
 - effect of radiation or 6-mercaptopurine: 21
 - virus-like particles, mouse: 1032, 1203, 1459
 - ^{90}Sr , swine: 26
- RADIATION LEUKEMOGENESIS, HUMAN
 - children, prenatal irradiation, latent periods: 2169
 - Hodgkin's disease, chromosomes: 1405, 1460
 - Japan
 - clusters (Hiroshima, Nagasaki and other cities): 2095
 - diagnostic or therapeutic irradiation: 18, 19, 561, 2166, 2167, 2168, 2604
 - Hiroshima and Nagasaki: 19, 592, 1672, 1756, 2165, 2602, 2603
 - occupational radiation exposure: 2166, 2167
 - perinatal and congenital, twins, review: 2136
 - ^{32}P , chromosomes: 1031
 - Ph^1 -positive chronic myeloid leukemia: 2635
 - review: 586
- RADIOACTIVE ISOTOPES AND ELEMENTS
 - cerium hydroxide dust containing radon, lung tumors, rat: 2171

RADIOACTIVE ISOTOPES AND ELEMENTS (contd.)

- ⁶⁰Co, leukemia, chromosomes, mouse: 1033
- ¹²⁵I or ¹³¹I
 - thyroid tumors, rat: 2132, 2175, 2257, 2265
- ¹³¹I
 - thyroid tumor, human: 30
 - with propylthiouracil, thyroid tumors, rat: 429
- ³²P
 - effect on WBC chromosomes, polycythemia vera: 1031, 2641
 - mouse leukemia: 1228, 1454
 - virus-like particles: 1032
- ²¹⁰Po
 - tobacco, smoking and lung cancer, review: 1024
- ²³⁹Pu
 - distribution, effect of oophorectomy, rat: 2299
 - endocrine tumors, rat: 2177
 - lung tumors, rat: 2176, 2177
- ⁸⁵Sr and ⁹⁰Sr
 - retention, dosimetry, dog: 1753
- ⁹⁰Sr
 - bones and teeth, USSR (all ages): 1453
 - leukemia, mouse: 2355
 - swine: 26
- thorium
 - bile duct cancer, human: 2170, 2172
- ADIOMIMETIC COMPOUNDS
 - chromosomal abnormalities, review: 1716
- ECTUM NEOPLASMS
 - epidemiology
 - appendectomy, West Germany: 2587
 - California (Los Angeles), ethnic groups: 2556
 - Jamaica: 2557, 2622
 - Tennessee (Nashville), ethnic groups: 2555
 - pathogenesis, single- or multiple-"hit" mathematical model: 2085, 2086
 - polyps
 - risk of malignant transformation, review: 1449
 - smoking: 1485
- ESERPINE
 - effect on
 - dimethylaminoazobenzene hepatoma, rat: 206
 - fluorenyldiacetamide liver tumors, mouse: 1856
 - tryptophan metabolism, smokers: 1099
- ESINS
 - intermediates in acetone or phenol production, skin tumors and leukemia, animal: 2304
- ESORCINOL
 - mutagenesis and effect on tumor incidence, *Drosophila*: 626
- ESPIRATORY CARCINOGENESIS
 - diethylnitrosamine, hamster: 208
 - dimethylbenzanthracene, hamster: 207
- ESPIRATORY DISEASES
 - bronchial epithelial cell abnormalities, smokers and other persons: 684, 2319
 - bronchitis
 - air pollution, data evaluation methods: 2537

RESPIRATORY DISEASES (contd.)

- epidemiology, Great Britain (including Scotland), air pollution and smoking: 2535, 2536
- non-malignant, epidemiology, tobacco processing workers, Poland: 172
- RESPIRATORY NEOPLASMS
 - epidemiology
 - environmental temperature, geographical variations, U.S.: 1343
 - India (Bombay), ethnic groups: 2066, 2067
 - Italy (Genoa): 905
 - occupational arsenic exposure, U.S.: 926
 - Switzerland, smoking: 128
 - multiple primary, smoking: 931
 - risk of second primary tumor, New York: 1665
 - upper respiratory tract and mouth cancer, smoking, U.S.: 1337
- RESPIRATORY TRACT
 - dye retention, effect of smoking, human: 173
 - toxicity
 - beryllium ores, monkey or hamster: 678
 - cigarette smoke, animal: 687
 - human: 683
 - tracheobronchial tree, age-related gland development, conventional or germ-free mice: 2102
- RETICULOENDOTHELIAL NEOPLASMS
 - aberrations of group 17/18 chromosomes, review: 1015
 - familial reticuloendotheliosis, SV40-transformation susceptibility of skin fibroblasts: 1225
 - possible induction by immunosuppressive therapy (kidney transplants): 2087
- RETICULOENDOTHELIAL SYSTEM
 - function, transplanted mammary tumors, mouse: 2646
 - macrophages, age-related herpesvirus resistance, mouse: 876
 - splenectomy and anticoagulants, effect on transplanted tumor, mouse: 622
 - thymectomy, effect on virus-induced mammary nodule or tumor induction, mouse: 820, 821
 - WBC phagocytic activity, effect of carcinogens, rat: 1180
- RETRORSINE
 - toxicity, liver, monkey: 2298
- RIBOFLAVIN
 - effect on
 - dimethylaminoazobenzene liver tumors, rat: 1940
 - liver phospholipids, dimethylaminoazobenzene hepatoma, rat: 1139
- RIFAMPICIN
 - effect on sarcoma virus production and transformation, chick embryo cells: 794
- RUBBER
 - dust
 - effect on tumor cells or tobacco callus *in vitro*: 1124
 - occupational exposure (shoe manufacturing), nasal cavity and sinus tumors, England (Northamptonshire): 1658
 - manufacturing, bladder cancer, Britain: 544, 927, 1119

RUBBER ADDITIVES

- nitrosoquinolines, s.c. tumors, rat: 39
- polymerized, effect on bladder, rat: 606

SACCHARIN

- bladder tumors, mouse: 1780
- effect on g.i. tract, mouse: 2315

SAFROLE

- liver and lung tumors, mouse: 1779

SALIVARY GLAND

- DNA, effect of isoproterenol, rat: 1930
- submaxillary, epithelial growth factor, effect on mouse mammary tumors in vitro: 139

SALIVARY GLAND NEOPLASMS

- epidemiology
 - environmental factors, U.S.: 1663
 - Sweden (Stockholm): 2584
- incidence of breast cancer and other second primary tumors: 338
- Induction
 - dimethylbenzanthracene, rat: 1072, 1073, 1812, 1814
 - fluorenylacetamide, rat: 1842
 - N-(4-[5-nitro-2-furyl]-2-thiazolyl)acetamide, rat: 1510

SALMONELLOSIS

- effect on aflatoxin toxicity, chicken: 749

SAPONIN(S)

- myelofibrosis with myeloid metaplasia, rabbit: 1163

SCAR TISSUE (See also under Injuries)

- achalasia of cardia or chemical burn, cancer of esophagus: 360, 1457, 1741, 2159, 2160
- alcoholic cirrhosis of liver, malignant transformation: 1415
- benign syphilis, penis cancer: 1401
- bone, sarcoma at site of injury, Paget's disease: 1404
- brain injury, malignant transformation, child: 1738
- bronchial scleroderma, malignant transformation, case and review: 2153
- burn scar, malignant transformation, skin: 1458
- esophageal or pharyngoesophageal diverticulum, malignant transformation: 1000, 2669, 2670
- fibromatosis and desmoids, familial: 543
- gastrectomy
 - or gastroenterostomy, esophagus cancer: 1045
 - stump, risk of stomach cancer, Hungary or Poland: 358, 359
- lung
 - antisera-induced, effect on nitroquinoline oxide lung tumors, mouse: 1475
 - pathology of lung scar cancer, human: 1043, 1044
- lupus vulgaris, malignant transformation, sun exposure or radiotherapy: 595
- peptic ulcer, stomach cancer: 596, 939
- phagedenic or rodent ulcer, malignant transformation, skin cancer: 24, 332, 988, 2666
- radiation injury, malignant transformation, skin: 1740, 1743
- skin, malignant transformation: 2158, 2162, 2666

SCAR TISSUE (contd.)

- therapeutic fluoroscopy and/or pneumothorax (for TB), cancer risk: 1748
- trachea (irradiated tracheal cancer), transformation, esophagus cancer: 593
- vaginal pessary implantation, malignant transformation: 1456
- varicose ulcer, malignant transformation, reticulum cell sarcoma after radiotherapy: 1745

SELENIUM

- effect on skin carcinogenesis, mouse: 1486

SEROTONIN

- fluorenylenebisacetamide-induced liver and intestinal tumors, rat: 1857

SEX CHROMOSOMES

- breast cancer: 955
- female genital cancer: 955, 2661
- mosaicism
 - XY/XO, with other chromosome abnormalities, acute myeloid leukemia: 954
 - XX/XXY (Klinefelter's), with lung cancer, SV40 transformation of WBC and fibroblast cultures: 2456
- relationship to trophoblastic proliferation, hydatidiform mole: 331
- testicular teratomas from male or female embryo grafts, mouse: 957

SEX DIFFERENCE

- adenovirus-12 tumor incidence, hamster: 122
 - aflatoxin kidney tumors, rat: 363
 - metabolism, rat: 668
 - benzpyrene metabolism, liver microsomes, rat: 643
 - cancer epidemiology, England/Wales and western Europe: 1389
 - colon/rectum cancer mortality, theoretical model: 2086
 - dimethylbenzanthracene effects, mouse or rat: 212, 1069, 1077
 - esophagus cancer, South Africa (Transkei), ethnic groups: 1386
 - familial cancer occurrence: 1679
 - fluorenyldiacetamide liver tumors, mouse: 1856
 - fluorobiphenylacetamide hepatoma, rat: 1509
 - gallbladder cancer with cholelithiasis, East Germany: 130
 - growth kinetics of Ehrlich ascites carcinoma, mouse: 137
 - hormone responsiveness of transplanted tumor, mouse: 1507
 - hydrazine sulfate liver or lung tumors, mouse: 1498, 1500
 - liver glycogen response to diethylnitrosamine, rat: 1531
 - melanoma epidemiology, England and Wales: 1683
 - plastic implant tumors, mouse: 2300
 - smoking-associated lung cancer
 - California (San Diego): 2541
 - Jews, Montreal or Pittsburgh: 2539, 2540
 - thyroid tumor size, radiation effects, human: 1029
- SHOPE FIBROMA VIRUS (See under Virus, pox)
- SHOPE PAPILLOMA VIRUS (See under Virus, papova)
- SILICA
- effect on herpesvirus infection, mouse: 875

ILICON

dust, occupational exposure, primary hemangio-
endothelial tumor of heart: 682

ILVER NITRATE

selective affinity of avian tumor viruses,
infected chicken cells: 783

IMAZINE (See s-Triazine, 2-chloro-3,6-bis
(ethylamino)-)

INAPYLALDEHYDE (See Cinnamaldehyde, 3,5-dimethoxy-
4-hydroxy-)

IN

aflatoxin distribution, rat: 1108

benzpyrene distribution, mouse: 1794

collagen, effect of methylcholanthrene, mouse:
222, 223, 224

dermatoglyphic patterns

children, leukemia, Poland: 916, 1391

retinoblastoma: 2108

dimethylbenzanthracene absorption, mouse: 1815

DNA, RNA and protein, effect of croton oil
factor A-1, mouse: 1564

intraepidermal nerve fibers, effect of
dimethylbenzanthracene, mouse or rabbit:
1818

mast cells, dimethylbenzanthracene uptake,
hairless strain mice: 1152

oral mucosa, benzpyrene uptake, hamster: 34

RNA, effect of benzpyrene, mouse: 380

proteins, bound dibenzanthracene metabolite,
analysis, mouse: 698

s.c. tissues

graft of stomach wall, sarcoma induction
by dimethylbenzanthracene, mouse: 215

migration of asbestos fibers, mouse: 1103

specific carcinogen-binding protein, analysis,
mouse: 2221

toxicity

aflatoxins, rabbit: 669

benzfluoranthene or tribenzfluoranthene,
mouse: 2237

tobacco smoke condensate, human: 691

transplantation, graft survival time, mouse
with urethan-induced lung tumors: 1838

IN CARCINOGENESIS

acridine orange

mouse: 237

aminoanthracene

dermal collagen synthesis, rat: 1466

aminofluorene derivatives

mouse: 1183

amphibian, review: 2157

anisoles

mechanism, review: 351

aromatic hydrocarbons and phorbol ester

mouse: 1784

arsenic

human: 1776

benzanthracene

cocarcinogen effects on threshold response,
mouse: 1087

derivatives, mouse, structure-activity
relationship: 1187

benzpyrene (mouse): 920, 1078, 1087, 1486, 2237

derivatives, chlorinated mouse: 602

bioassay of very weak carcinogens, new mouse
strain: 1190

SKIN CARCINOGENESIS (contd.)

bis(chloromethyl)ether

mouse: 419

coumarin compound (detergent additive)

radiation effects, mouse: 2301

dibenzanthracene or dibenzpyrene

accelerated induction method, mouse:
384

dimethylbenzanthracene

hamster cheek pouch: 373, 694, 695, 696,
697, 1075, 1076, 1802, 1813, 1926, 2225,
2229, 2230

mouse: 35, 45, 46, 47, 208, 237, 378,
1067, 1078, 1079, 1486, 1513, 1521,
1803, 1815, 2157, 2329

rat: 44, 212

diphenylpropynyl-N-cyclohexylcarbamate

s.c. sarcoma or Zymbal's gland tumor, rat:
563

estradiol

rat: 707

ethylnitrosourea

fetal pig: 249

fluorenylacetamide

effect of sunflower oil, rat: 1842

halogenated ethers

mouse: 419

hexamethylbenzene

mouse: 1478

initial epidermal stages of 2-stage carcino-
genesis, mouse: 1188

γ -irradiation

effect of UV, mouse: 1744

mammals, review: 2124, 2127, 2157

medicinal wax (ozokerite ceresin)

mouse: 2307

methylcholanthrene

amphibia (*Bufo arenarum*): 1056

mouse: 48, 222, 223, 224, 256, 389, 391,
392, 393, 537, 1054, 1055, 1057, 1058,
1067, 1078, 1486, 1565, 2182, 2186,
2191, 2195, 2197

virus-like particles: 1896

rat: 659, 707

squirrel monkey: 700

transplanted tumors, karyotype, hamster:
221

3-methyltricycloquinazoline

mouse: 2271

naphthalene derivatives

mouse: 1183

N-(4-[5-nitro-2-furyl]-2-thiazolyl)acetamide

rat: 1510

nitroquinoline oxide

mouse: 229

phenanthro(2,1- α)thiazole

and its 2-methyl analog, mouse: 1470

β -propiolactone

mechanism, mouse: 1921

pyrolytic resins

intermediate in acetone or phenol production,
mouse or rabbit: 2304

radiation

human: 25, 1452, 1743

mouse: 168, 2299

rabbit: 1028

SKIN CARCINOGENESIS (contd.)

- rat: 1038
- role of intramitochondrial dense bodies, mouse: 2184
- s.c. tumors
 - aflatoxin analog (afutoxin), mouse: 1488
 - amino- or nitrodibenzpyrene, mouse: 386
 - antitumor antibiotics (actinomycins or mitomycin C), mouse: 1539
 - antitumor agent (ibenzmethylin), rat: 605
 - avian adenovirus (CELO), hamster: 2511
 - azuleno(5,6,7-cd)phenalene, mouse: 1546
 - benzpyrene
 - attempted induction, cattle: 1068
 - primate: 50
 - cadmium, enzymes, rat: 235
 - carboxynitroquinoline oxide-transformed cells, hamster: 2274
 - carcinogen-treated lung explants, mouse: 1462
 - cholesterol or glycerol polymers, mechanism, rat: 1544
 - dibenzpyrene, mouse: 1214
 - 1-(4-dimethylaminobenzal)indene, rat: 53
 - dimethylbenzanthracene
 - hamster: 1816
 - mouse: 49, 611
 - primate: 50
 - rat: 2264
 - effect of CNS-acting treatment, rat: 2192
 - fatty acids, mouse: 1494
 - heated edible fats and oils, rat: 241
 - hydroxycholesten-3-one, mouse: 1936
 - hydroxyxanthine, mouse or rat: 1161
 - iron dextran, rat: 233
 - methylcholanthrene
 - attempted induction, cattle: 1068
 - mouse: 40, 41, 42, 51, 611, 657, 658, 1063, 1064, 1512, 1514, 1515, 1516, 1541, 1900, 2183, 2196
 - rat: 1502, 2190, 2193, 2194
 - mineral oil, transplantation, mouse: 1492
 - 4-nitroquinoline, mouse: 422
 - nitroquinoline oxide
 - rat: 674
 - transformed embryonic cell cultures, rat: 1166
 - nitrosoquinoline derivative (rubber additive), rat: 39
 - oral contraceptive, rat: 1830
 - plastics
 - blood supply, rat, review: 2117
 - karyotype, strain and sex differences, mouse: 2300
 - radiation effects, rat or dog: 2299
 - rat: 1132, 1543
 - polyethylene, rat: 38
 - polyoma virus + fluorenylacetamide, synergism, rat: 1202
 - printing inks, mouse: 607
 - purine N-oxides, structure-activity relationship, rat: 1189
 - radiation, rabbit: 1028
 - spontaneously transformed rat embryo cell cultures, karyotype: 2628
 - rubber additive, rat: 606

SKIN CARCINOGENESIS (contd.)

- surgical adhesives, strain differences, mouse: 2306
- transplanted methylcholanthrene-treated lung cultures, mouse: 1897
- screening method
 - mouse: 1463
- scrotum
 - occupational mineral oil exposure: 1767
- Shope papilloma virus
 - fetal and adult rat: 1327
 - mechanism, rabbit: 1609
- soil extracts
 - low or high benzpyrene content, mouse: 2213
- stilbene derivatives (detergent additives)
 - radiation effects, mouse: 2301
- sunlight
 - pathogenesis: 2161
- tobacco preparations
 - hamster: 1802, 1842
 - mouse: 35, 45, 174, 175, 176, 177, 688, 689, 692, 1096, 1097, 1098, 1784, 1803
- s-triazine compounds
 - mouse or rat: 2272
- tumor promotion
 - unburned tobacco extracts, mouse: 1542
- urethan and related compounds
 - mouse: 58, 1186
- vitamin A palmitate
 - lymphoma-like tumors, hamster cheek pouch: 1164
- SKIN DISEASES
 - familial, malignant transformation: 1742
 - plantar or palmar keratoses, cancer pts. and normal subjects: 2109
 - von Recklinghausen's disease, relationship to neuroblastoma, child: 2656
- SKIN NEOPLASMS
 - amphibian
 - melanoma, seasonal incidence, Triturus: 628
 - dogs
 - epidemiology, USSR (Moscow): 2098
 - eccrine sweat duct tumors, benign and malignant, differentiation: 968
 - epidemiology
 - age factors, Germany (Giessen): 1365
 - India, Hindus and Parsis, Bombay: 2066, 2067
 - Saurashtra: 1364
 - Minnesota: 1355
 - Nigeria: 1667
 - sunlight: 2161, 2529
 - familial basal cell nevus syndrome, radiation-induced maxillary cancer: 2163
 - fish
 - melanoma, effect of amino acids on DNA: 334
 - papilloma
 - Atlantic eel (Anguilla vulgaris): 2667
 - San Francisco Bay, species specificity, water pollution: 534
 - heredity, review: 15
 - Kaposi's sarcoma
 - associated chronic leukemia, pathogenesis: 1707

KIN NEOPLASMS (contd.)

- epidemiology, Nigeria: 1371
- malignant transformation of
 - calcifying Malherbe's epithelioma: 2657
 - epidermodysplasia verruciformis, virus particles: 2501
 - hereditary skin diseases: 1742
 - herpes infection or traumatic scar, lip cancer: 594
 - hidradenitis suppurativum: 1417
 - lupus vulgaris scars, radiotherapy or sun-light exposure: 595
 - phagedenic ulcer of leg, Senegal: 24, 332
 - radiation dermatitis: 1740, 1743
 - rodent ulcer: 988, 2666
 - scar tissue: 594, 595, 1458, 1740, 1745, 2158, 2162, 2666
 - xeroderma pigmentosum: 1742
- melanoma
 - epidemiology
 - England and Wales, sex difference: 1683
 - Nigeria: 1683
 - familial: 533
 - malignant transformation of benign or epithelial nevus: 558, 2671
 - nuclear RNA fractionation: 950
 - sun exposure, Australia: 558, 1381
- mouse
 - genetic susceptibility or resistance, epidermal cell endoplasmic reticulum, mouse: 1422
- neurofibromatosis, familial patterns of freckling: 1413
- nevus sebaceus, risk of supervening malignant tumor: 2527
- occupational
 - epidemiology, Britain: 889
 - medicolegal review: 1717
- photochemical repair defect: 170
- premalignant
 - Bowen's disease, virus-like particles: 1295
 - or malignant, chromosomes, human: 342, 923
- rabbit
 - Shope papilloma virus-induced, mitotic activity during keratinization, rabbit: 2473
- rat
 - differentiation of tumor stem cells: 1421
 - risk, second primary tumor, New York: 1665
 - ulcus terebrans, classification: 988
- SOCIOECONOMIC FACTORS
 - cancer epidemiology, relationship to smoking habits: 2070
 - cervix cancer, review: 1721
 - stomach cancer,
 - England and Wales: 1661
- SODIUM CHLORIDE
 - benzpyrene content, drying methods: 2210
- SOL
 - anaerobic bacteria, benzpyrene synthesis: 600
 - benzpyrene content
 - airport area, USSR (Moscow): 2212
 - bioassay (mouse skin): 2213
 - industrial or rural region, USSR: 1787, 1792

SOIL (contd.)

- petroleum processing plant, USSR: 1086
- uptake of benzpyrene by plants: 1086, 1787, 1792, 2212
- microorganisms, geographical cancer distribution, U.S.: 1647
- SORBIC ACID
 - effect on connective tissue, rat: 699
- SPIRONOLACTONE
 - effect on
 - dimethylbenzanthracene adrenal necrosis, rat: 375
 - mammary tumors, rat: 2227
- SPLEEN
 - antibody localization, Moloney virus-induced lymphoma, mouse: 770
 - dimethylbenzanthracene-DNA binding, rat: 1801
 - gallium distribution, leukemic or nonleukemic AKR/J mice: 1775
 - pathology
 - Friend leukemia virus infection, mouse: 765, 1306, 1637
 - Graffi viral leukemia, mouse: 1224
 - Rauscher viral leukemia, mouse: 2349
 - polyoma virus-infected mouse: 1311
- STATOLON
 - effect on
 - Friend viral leukemia, mouse: 1321, 1971
 - Moloney sarcoma or Friend leukemia virus in vitro: 1235
 - spontaneous tumors, virus-positive mouse strains: 1573
- STEARIC ACID DERIVATIVES
 - s.c. sarcoma, mouse: 1494
- STERIGOMATOCYSTIN
 - toxicity, liver, monkey: 2258
- STEROLS
 - analysis, ethyl- or methyl nitrosourea-induced brain tumors, rat: 1881
- STILBENE, 4-ACETAMIDO-
 - metabolism, rat: 245
- STILBENE, DIMETHYLAMINO-
 - skin tumors, effect on methylcholanthrene carcinogenesis, rat: 659
- STILBENE, N-HYDROXY-4-ACETAMIDO-
 - metabolism, rat: 245
- STILBENE, N-HYDROXY-4-ACETYLAMINO-, ACETIC ACID ESTER
 - mutagenesis, bacteria: 2239
- STILBENE DERIVATIVES
 - detergent additives, skin tumors, radiation effects, mouse: 2301
- STOMACH
 - DNA, methyl nitro-N-nitrosoguanidine uptake, rat: 1872
 - intragastic nitrosamine formation from dimethylamine, mechanism: 639, 1529
 - s.c. graft, sarcoma induction by dimethylbenzanthracene, mouse: 215
- STOMACH NEOPLASMS
 - associated
 - ataxia-telangiectasia, familial: 552
 - peptic ulcer and atherosclerosis: 2110
 - cell lines (MC-8 or MC-12) with EB virus, human: 299

STOMACH NEOPLASMS (contd.)

- epidemiology
 - air pollution, bioassay method: 1791
 - Armenian SSR (Yakutsk): 2548
 - Colombia (Cali), ethnic groups, intestinal metaplasia: 1390
 - dietary carcinogens, review: 1014
 - proteins, international: 1432
 - England and Wales, environmental factors: 1661
 - Iceland, dietary factors: 2083
 - Japan
 - air pollution and smoking, Tokyo: 1657
 - geographical variations, Osaka and Nara prefectures: 2546
 - peptic ulcer: 1662
 - relationship to leukemia: 2601
 - Kenya (western) and Tanzania (northwestern): 2520
 - mathematical models: 896
 - Minnesota (Minneapolis), pernicious anemia: 2551
 - Natal (Durban), ethnic groups, betel chewing: 1656
 - Poland: 897, 1373, 1375, 2550, 2623
 - smoking: 542
 - review: 532
 - Rumania, urban and rural: 2515
 - Utah, geographical variations: 2552
 - Uzbekh SSR, ethnic groups, geographical variations: 2547
 - West Germany, appendectomy: 2587
 - Yugoslavia, geographical variations: 2549
- etiology, possible, nitrate reduction to nitrosamine by gastric bacteria, human: 639, 1529
- growth rate, role of intestinal metaplasia or ulceration: 939
- induction
 - benzpyrene, mouse: 1791
 - dibutyl nitrosamine, mouse: 248
 - fluorenylacetamide, rat: 1842
 - hydroxyaminoquinoline oxide, rat: 428
 - methylcholanthrene, guinea pig: 1899
 - N-methyl-N'-nitro-N-nitrosoguanidine, rat: 1873, 1874, 1875
 - nitrosopiperidine, mouse: 67
 - radiation, mouse: 167
- malignant transformation of
 - familial polyposis (Peutz-Jeghers), child: 962
 - gastric stump, risk, Hungary or Poland: 358, 359
 - peptic ulcer: 596, 939
 - occupational pesticide exposure, case and review: 1720
 - risk of multiple primary tumors: 1359
- STOMACH ULCER (See Ulcer, peptic)
- STREPTOZOTOCIN (See N-Nitrosourea, N-methyl-, 2-deoxy-D-glucose derivative)
- STRESS (See also under Injuries)
 - cold, effect on dimethylbenzanthracene salivary gland tumors, rat: 1072
 - crowding, effect on dimethylbenzanthracene mammary tumors, rat: 1070

STRESS (contd.)

- effect on
 - animal tumors, review: 1711
 - Friend leukemia virus infection, mouse: 96
- electrical current, tumor stimulation, rat: 1750, 2181
- noise, effect on methyl dimethylaminoazobenzene liver tumors, rat: 2180
- rotary motion, effect on methyl dimethylaminoazobenzene liver tumors, rat: 2179
- surgical trauma (mastectomy), effect on dimethylbenzanthracene mammary tumors, rat: 1071

SUCROSE

- effect on g.i. tract, mouse: 2315

SULFATE ION

- effect on hydroxyfluorenylacetamide metabolism, rat liver: 672

SULFUR DIOXIDE

- air pollution, effect on arsenic exposure as respiratory carcinogen, human: 1699

SUNFLOWER OIL (See under Oils, edible)

SURGERY

- appendectomy
 - cancer risk, West Germany: 2587
 - or tonsillectomy, cancer risk, New York (Kings County): 2586
- SV20 (See under Virus, adeno-)
- SV40 (See under Virus, papova)

TANNIC ACID

- effect on protein synthesis, rat liver: 1179

TEETH

- odontogenic epithelium, polyoma virus transformation, mouse embryo: 1274
- ⁹⁰Sr levels, USSR (all ages): 1453

TEMPERATURE

- cold stress, effect on dimethylbenzanthracene salivary gland tumors, rat: 1072
- effect on antigens and thymidine kinase, SV40-infected cells: 874
- environmental, cancer mortality, geographical variations, U.S.: 1342, 1343
- high
 - inactivation of Yaba monkey poxvirus: 868
- reproduction and viability of transformed cells: 500
- low
 - effect on surface antigens, EB virus-positive Burkitt lymphoma cell lines: 1617
 - virus development, Lucké renal adenocarcinoma, frog: 2492
 - refrigeration, effect on aflatoxin production, *Aspergillus flavus*: 661
 - sensitive mutants of avian sarcoma virus (B77), properties: 1962
- TEMPERATURE, BODY
 - diurnal changes, normal and tumor-bearing rat: 2652
- TERATOGENESIS (See also under Embryo)
 - aflatoxins, alkylating agents and nitroso compounds, animal: 1859

- TERATOGENESIS (contd.)
 benzanthrane derivatives, structure-activity relationship, rat: 1807
 carcinogens, animal, review: 2129
 mathematical model, review: 2130
- TESTIS NEOPLASMS
 differentiation of tumor stem cells: 1421
 embryonal carcinoma, serum α -fetoprotein, review: 2134
 epidemiology
 Denmark, urban and rural: 936
 Finland: 2578
 homology to tumors of ovary: 1383
 interstitial cell
 diethylstilbestrol induction, mouse: 73
 mixed (Sertoli cell), possible estrogen synthesis, mouse with mammary tumor: 152
 steroid biosynthesis, mouse: 1506
 lead acetate induction, rat: 1131
 occurrence, possible genetic or viral influence, Mexican axolotl (*Ambystoma mexicanum*): 2650
 teratoma
 from male or female embryo tissue grafts, sex chromosomes, mouse: 957
 induction, transplanted embryonic genital ridge, mouse: 1703
 spontaneous, mouse leukemia virus-containing, mouse: 1231
 pathology, mouse or rabbit: 1231
 Yaba poxvirus-induced, monkey, isolation and properties of virus: 1290
- TESTOSTERONE
 effect on transplanted tumor, sex difference, mouse: 1507
 leiomyosarcoma of ductus deferens, autonomous hormone-independent lines, hamster: 1130
 myelomonocytic leukemia, chromosomes and muramidase, mouse: 406
 with methylcholanthrene, prostate tumors, histochemistry, mouse: 716
- TESTOSTERONE PROPIONATE
 effect on
 dimethylbenzanthracene tumors, rat or mouse: 1128, 1822
 transplantable mammary tumors, mouse: 2267
- TESTOSTERONE PROPIONATE + DIETHYLSTILBESTROL
 implantation, uterine leiomyosarcoma, hamster: 1833
- TEXTILES
 manufacturing
 air pollution, lung cancer, England and Wales: 1660
 stomach cancer, England and Wales: 1661
- THALIDOMIDE
 effect on methylcholanthrene skin tumors, mouse: 1058
 mutagenesis and effect on tumor incidence, *Drosophila*: 626
- THIAZOLE, 2-(2-FORMYLHYDRAZINO)-4-(5-NITRO-2-FURYL)-
 mammary, kidney, liver or g.i. tumors, rat: 1548
- THIOURACIL, 6-METHYL-
 effect on ^{131}I thyroid carcinogenesis, rat: 2257
- THIOURACIL, 6-METHYL- (contd.)
 hormone imbalance, effect on methylnitrosourea-induced brain tumors, rat: 2284
 thyroid tumors
 effect of electrical injury, rat: 2181
 ultrastructure, hamster: 726
- THIOUREA
 toxicity, lung, mouse: 701
- THOROTRAST (See under Radioactive isotopes and elements)
- THYMINE ALKYLAMINE (See under Antitumor agents)
- THYMUS
 cell cultures, transformation, nitrosoguanidine derivative, rat: 424
 gallium distribution, leukemic or nonleukemic AKR/J mice: 1775
 graft
 effect on methylcholanthrene s.c. tumors, mouse: 41
 tumor immunity, induced sarcoma, mouse: 42
 lymphoma induction, Gross leukemia virus-infected mouse: 1646
 Gross leukemia virus-transformed rat cells, pathology: 2065
 growth kinetics, radiation-induced leukemia, mouse: 2164
 immunity, leukemogenesis, review: 991
 methylnitrosourea toxicity, mouse: 1557
 thymectomy
 effect on
 dimethylbenzanthracene leukemia or skin tumors, mouse: 1077, 1809
 host immunity, thymoma-bearing mice: 1198
 radiation leukemogenesis, mouse: 2355
 urethan lung tumors or lymphoma, mouse: 1083, 1841
- THYMUS NEOPLASMS
 dimethylbenzanthracene
 lymphoma, alkaline phosphatase, mouse: 2389
 thymoma, host immunity, effect of thymectomy, mouse: 1198
 Graffi virus leukemia, pathogenesis, mouse: 1224
 induction
 dimethylurea + nitrite, rat: 1882
 ethylnitrosourea, strain A mice: 2282
 Gross-leukemia virus-infected mouse, thymic graft lymphoma: 1646
 hydroxylaminoquinoline oxide, rat: 428
 6-mercaptopurine, cell-free transmission, mouse: 1552, 2389
 methylcholanthrene, cell-free passage, mouse: 1552
 Moloney leukemia virus-transformed rat thymus cells, rat: 2356
 radiation-induced
 DNA replication, mouse: 29
 effect of diet, mouse: 1461
 transplantable, functioning as normal thymus, mouse: 431
- THYROID
 dimethylbenzanthracene thyroiditis, rat: 213
 goitrogenic capacity, radiation effects, rat: 2174

THYROID (contd.)

- growth curve, effect of goitrogen, rat: 333
- human, cells, effect of SV40 infection: 1284
- methylcholanthrene-induced thyroiditis, pathology, rat: 1050
- mouse strains with high or low ¹³¹I uptake: 2644

THYROID NEOPLASMS

- benign or malignant, factors affecting malignancy, animal, review: 2119
- complication of ¹³¹I therapy of thyrotoxicosis: 30
- epidemiology
 - Hawaii (Oahu): 2074
 - Israel: 883
 - Minnesota (Olmsted County; Rochester): 887
 - radiation exposure, Japan (Hiroshima/Nagasaki): 930
 - New York (Rochester): 2173
 - review: 584
 - sarcomas, Italy: 913
 - sex ratio, England/Wales and western Europe: 1389
 - South Korea: 1686
 - world, review: 2133
- frequency of double or multiple primary tumors: 143

induction

- dimethylurea + nitrite, rat: 1882
- ¹²⁵I or ¹³¹I, rat: 2175
- ¹³¹I, effect of methylthiouracil, rat: 2257
- and low-iodine diet, effect of hypophysectomy, rat: 2265
- lead acetate, rat: 1131
- methylnitrosourea, rat: 37
- methylthiouracil, hamster: 726
- and hemithyroidectomy, effect of electrical injury, rat: 2181
- propylthiouracil and ¹³¹I, rat: 429
- transplanted iodine-deficient goiter, rat: 2266, 2629
- malignant transformation of cold nodules, risk: 1705

medullary carcinoma

- with amyloid stroma, epidemiology, Switzerland (Lausanne): 2585
- with epinephrine-producing pheochromocytoma, familial: 948

radiation-induced, rat, review: 2132

sex difference in tumor size, radiation effects, human: 1029

spontaneous, strain differences, rat: 1433

THYRONINE, L-3,5,3'-TRIiodo-

- inhibition of methylcholanthrene s.c. sarcoma: 1502

TOBACCO

Aspergillus cultures, aflatoxin production:

- 748
- carcinogens, chromosomal abnormalities, review: 1716
- chewing, oral and pharyngeal cancer, India: 935, 2531
- cocarcinogens, cell culture test: 1761
- extracts, antigenicity (human serum): 1769
- heavy metal content (lead, cadmium, nickel): 686

TOBACCO (contd.)

- hybrid strain (Nicotiana glauca x N. langsdorffii), tumor induction, tobacco smoke condensate: 2322
- occupational exposure, respiratory diseases, Poland: 172
- powdered, lung or liver tumors and leukemia, mouse: 2318
- snuff
 - nasal cavity tumors, historical review: 2115
 - occupational dust exposure (shoe factory and bakery workers), England (Northamptonshire): 1658
- unburned, tumor-promoting substances, mouse skin: 1542

TOBACCO SMOKE

- adaptation, effect on nitroquinoline oxide or nitroquinaldine oxide cytotoxicity, marine plankton: 414
- analysis, nitrogen compounds, review: 2156
- bioassay, method, mouse tumor cell cultures: 1545
- ciliostasis, effect of metaproterenol, rabbit trachea in vitro: 2323
- cocarcinogenesis, skin, mouse: 35
- containing Cannabis constituents, analysis: 1765
- effect on
 - liver xoxazolamine hydrolase, hamster and rat: 180
 - mitochondria, Tetrahymena: 1483
- extracts
 - lung tumors, mouse: 1768
 - tumor promotion or induction, hamster cheek pouch or skin: 1802, 1842
- filtered
 - abnormal growth patterns and chromosomes, mouse lung or kidney cells: 1211
 - or unfiltered, heavy metal content (lead, cadmium, nickel): 686
- inhalation, chronic toxicity, animal: 687
- skin tumors, mouse: 35, 45, 174, 175, 176, 177, 688, 689, 692, 1096, 1097, 1098, 1784, 1803
- toxicity
 - bronchus: 737
 - lung, measurement method, mouse: 2317
 - rabbit trachea in vitro: 2323
 - skin, human: 691
 - tumor induction, hybrid tobacco plant: 2322

TOBACCO SMOKING

- bladder cancer: 690
- U.S.: 2544
- brain tumors
 - Minnesota: 2580
- bronchial epithelial cell abnormalities, classification: 2319
- cancer epidemiology
 - India (Bombay), Hindus and Parsis: 2066, 2067
 - relationship to socioeconomic status: 2070
 - review: 1714, 1715
 - U.S.: 1337, 2071
- consumption rates 1910-1965, Denmark: 936
- effect on
 - asbestosis induction, review: 1713

TOBACCO SMOKING (contd.)

- dye retention, human respiratory tract: 173
- larynx, human: 178
- mucociliary efficiency of lung, human: 1770
- oral fluid cells, human: 413
- photochemical repair, human oral mucosa: 170
- placental aryl hydrocarbon hydroxylase activity, human: 685
- urinary chemiluminescence, bladder cancer etiology: 1100
- niacin metabolites: 1484
- tryptophan metabolites: 1099, 1484
- esophagus cancer
 - Africa (high- or low-incidence nations) and U.S. (nonwhite): 1698
 - Puerto Rico: 932
 - South Africa, ethnic groups: 928
- g.i. cancer, Poland: 542
- health hazard, review (book): 166
- larynx cancer, Czechoslovakia: 881
- life expectancy, U.S. men: 900
- lip cancer, U.S.: 2530
- lung cancer
 - ABO blood groups: 904
 - California (San Diego), sex difference: 2541
 - East Germany: 526, 2543
 - Hungary (Szeged): 1654
 - Iceland: 1653
 - international: 179
 - Italy: 325
 - Japan (urban): 1657, 2538
 - Jews, sex difference, Montreal or Pittsburgh: 2539, 2540
 - ²¹⁰Po content of tobacco, review: 1024
 - review: 166, 569, 574, 1024, 1714, 1715, 2071
 - Scotland, coal miners: 1659
 - urban and rural: 2536
 - South Africa, ethnic groups: 901, 928, 1655, 2542
 - Switzerland: 128
 - treated TB: 1748
 - U.S.: 1337
- mouth cancer
 - India (rural): 935
 - Puerto Rico: 932
- multiple primary tumors of upper g.i. and respiratory tract: 931
- pharynx cancer, Puerto Rico: 932
- polyps of colon and rectum: 1485
- respiratory diseases
 - coal miners, Germany: 1117
 - epithelial hyperplasia or squamous metaplasia, human: 683, 684
 - Great Britain (including Scotland): 2535, 2536
 - Japan (Tokyo): 1657

-TOLIDINE

- poisoning, mechanism, rat: 2232

OLUENE DERIVATIVES

- occupational exposure, leukemia: 372

-TOLUENEDIAMINE

- liver tumors, effect of other carcinogens, rat: 2235

o-TOLUIDINE

- lung or kidney tumors, fetal mouse: 714

TOLUIDINE BLUE (See under Dyes and stains)

TONGUE NEOPLASMS

- epidemiology, Canada, urban and rural: 895

TONSILLECTOMY (See under Surgery)

TOXICITY

aflatoxins

- amphibian larvae: 1109
- chick embryo: 257, 1109
- chicken: 365, 749
- farm animals, review: 572
- human liver: 1914
- monkey: 1913, 2298
- mouse: 1915, 1938
- rabbit: 669
- rat: 699, 740, 1108, 1938
- salmon or trout, species difference: 666
- species difference, mechanism: 750

benzfluoranthene or tribenzfluoranthene

- mouse: 2237

benzidine and related compounds

- rat: 2232

benzpyrene

- mammalian fibroblasts, species difference: 2202

beryllium and beryllium compounds

- rodent or monkey: 678, 2312

carcinogenic antitumor agent (ibenzmethyzin)

- hamster: 605

cycasin and aglycone

- mouse or rat: 995, 1924

diethylnitrosamine

- liver, rat: 1148

dimethoxyaminoazobenzene

- rat: 1889

dimethylbenzanthracene

- mammalian fibroblasts, species difference: 2202

- mechanism, rat: 1210

dimethylnitrosamine

- monkey or dog: 1871

dimethyl-p-phenylazoaniline

- cockroach: 624

dimethylthionitrosamine

- rat: 247

evaluation methods, mathematical model,

- review: 2130

2-fluorenamine

- cockroach: 624

food coloring (Ponceau MX)

- liver, mouse: 609

hepatocarcinogens

- liver, mechanism, rat: 1860

hexamethylenetetramine

- mouse or rat: 608

hydrazine sulfate

- liver, hamster: 1500

isonicotinic acid hydrazide

- hamster: 421

lead acetate

- kidney, hamster: 720

methenamine

- rat: 1922

methylcholanthrene

- cockroach: 624

TOXICITY (contd.)

- methylnitrosamines and methylnitrosamides
 - mouse: 1185
- methylnitrosourea
 - thymus, lymph nodes and bone marrow, mouse: 1557
- phenylbutazone
 - rat: 1922
- photographic emulsion component or developing agent
 - rat or mouse: 2305
- pyrrolizidine alkaloids
 - liver, rat: 2308
- retrorsine
 - liver, monkey: 2298
- sorbic acid
 - connective tissue, rat: 699
- sterigmatocystin
 - liver, monkey: 2298
- tobacco smoke
 - animal: 687, 2317, 2323
 - human: 683, 691

TOYOCAMYCIN (See under Antitumor agents)

TRACHEA

- benzpyrene-induced squamous metaplasia, effect of citral or vitamin A in vitro, hamster: 1795

- tobacco smoke-induced ciliostasis, effect of metaproterenol in vitro, rabbit: 2323

TRACHEA NEOPLASMS

- cell growth kinetics, measurement method: 2614
- induction, dibutylnitrosamine, strain differences, hamster: 1537
- radiation cure, second (esophagus) and third (prostate) primary tumors: 593

TRANSPLACENTAL CARCINOGENESIS (See under Pregnancy)

TRAUMA (See Injuries)

TRIAZENE COMPOUNDS

- 1-aryl-3,3-dialkyltriazenes, mechanism of action, cell-free system: 1174
- structure-activity relationship, rat: 1193

TRIAZENE, PHENYLDIMETHYL-

- brain tumors, rat: 2269, 2270

- peripheral nerve tumors, rat: 636

s-TRIAZINE, 2-CHLORO-3,6-BIS(ETHYLAMINO)-

- g.i. and skin tumors, mouse or rat: 2272

s-TRIAZINE-2,4,6-TRIOL

- liver or skin tumors, mouse or rat: 2272

TRYPAN BLUE (See under Dyes and stains)

TRYPTOPHAN

• metabolism

- bladder cancer: 1195
- effect of pyridoxine or reserpine, smokers: 1099
- tumor recurrence rate, bladder cancer: 1162

TRYPTOPHAN METABOLITES

bladder cancer

- Boston or Wisconsin, urbanization: 70
- effect of ascorbic acid, mouse: 239, 423
- review: 5

- effect on DNase-II, cell-free system: 612

excretion

- bladder cancer: 690
- dietary factors, Africa (Uganda): 1368
- smokers: 1484

- metabolism, animal: 1931, 1932

ULCER, PEPTIC

- association with stomach cancer and atherosclerosis: 2110
- cancer of gastrectomy stump, Poland or Hungary: 358, 359
- geographical distribution, relation to stomach cancer, Japan: 1662
- malignant transformation (stomach cancer), human: 596, 939

URACIL, PROPYLTHIO-

- with ¹³¹I, thyroid tumors, rat: 429

URBANIZATION (See under Environmental factors)

UREA, 3-(p-CHLOROPHENYL)-1,1-DIMETHYL-

- effect on glycolysis, rat liver: 2263

UREA, DIMETHYL-

- heart, thymic, kidney or thyroid tumors, rat: 1882

URETHAN

- activation of mammary tumor virus, mouse: 818
- cytotoxicity, embryonic mouse lung cultures: 2290

effect on

- DNA and RNA, transplanted tumor or regenerating liver, mouse: 621
- polyoma virus-induced hemagglutinins, yeast: 1275
- virus-free preneoplastic mammary outgrowths, mouse: 1836

- epidermal hyperplasia, mouse skin: 1188

- immunosuppression, mouse: 1527

leukemia

- effect of leukemia virus, mouse: 2288
- partial hepatectomy, mouse: 2286
- Moloney or Rauscher leukemia virus-like particles, mouse: 1459

liver tumors

- effect of leukemia virus, mouse: 2288
- partial hepatectomy, mouse: 2286

- lung tumors (mouse): 410, 701, 1778, 1838, 1839, 1840

effect of

- butyl or isoamyl carbamate: 1082
- cortisone: 1081
- Freund's adjuvant: 677
- effect of germ-free status: 411
- immune serum: 1526
- influenza virus: 2291
- leukemia virus: 2288
- lymphoid cells: 59
- partial hepatectomy: 2286
- thymectomy: 1083, 1526, 1841

- with virus-containing leukemia: 1991

- radiation effects: 1039, 1081, 1841

lymphoma (mouse)

- chromosomes: 77, 238
- effect of thymectomy: 1083
- leukemia virus activation: 408
- tumor cell DNA: 1080
- virus-like particles: 75

- mammary tumors, mouse: 712

- melanoma of eye, rat: 629

- metabolism, effect of partial hepatectomy, mouse: 2285

- metabolites, mutagenesis, Drosophila: 2289

- related compounds, leukemia and skin or lung tumors, structure-activity relationship, mouse: 58

JRETHAN (contd.)

- skin tumors, mouse: 1186, 1188, 1463
- susceptibility, relationship to postnatal cell growth rate, lung, mouse or hamster: 2287
- toxicity, hamster (*Phodopus sungorus*): 2642
- transplacental, lung or kidney tumors, mouse: 714
- treated lung explant, s.c. tumors, mouse: 1462
- tumor induction, effect of influenza virus, mouse: 1619

JRETHAN, N-HYDROXY-

- cytotoxicity, embryonic mouse lung cultures: 2290

- melanoma of eye, rat: 629

JRETHAN ANALOGS

- butyl carbamate
 - effect on urethan lung tumors, mouse: 712
 - mammary tumors, mouse: 712
- N-hydroxycarbamates, skin tumor initiation, mouse: 1186
- isoamyl carbamate, effect on urethan lung tumors, mouse: 1082

JROKINASE

- effect on transplanted tumors, mouse: 2302

JTERUS NEOPLASMS (See Corpus uteri neoplasms)

VAGINA NEOPLASMS

- artificial vagina formed after surgery for cervical carcinoma, case: 2658
- induction
 - alkylnitrosoureas, pregnant rat: 713
 - plastics, mouse: 1836
- vaginal pessary: 1456

VASCULAR NEOPLASMS

- hemangioendothelial sarcoma, induction, 5-acetamido-3-(5-nitro-2-furyl)-6H-1,2,4-oxadiazine, rat: 426

VERRUCA VULGARIS VIRUS (See under Virus, pox)

VINBLASTINE (See under Antitumor agents)

VIRAL CARCINOGENESIS

- animal, review: 1728
- cellular antigens, review: 354
- cervix or prostate, review: 576
- chromosomal abnormalities, classification, review: 1002
- DNA viruses
 - chromosomes, review: 1732
 - mechanism, infected or transformed cells: 835
 - nuclear antigens, review: 1731
 - review: 577
- echovirus-12, -22, -23 and -29 (human)
 - hamster: 518
- genetic factors, theory, review: 1729
- hamster, parainfluenza-like viruses from British wild squirrels: 1299
- human adenoviruses, mechanism, review: 1730
- Moloney sarcoma virus, chicks and mammals: 2365
- possible, testicular tumors, Mexican axolotl (*Ambystoma mexicanum*): 2650
- reovirus type 3 (human), hamster: 518
- respiratory syncytial virus (human), hamster: 518

VIRAL CARCINOGENESIS (contd.)

- review: 2126, 2140, 2142, 2143
- RNA viruses
 - mechanism, review: 8, 577
- Rous sarcoma virus
 - (Carr-Zilber strain), mouse: 2371
 - (Schmidt-Ruppin strain) or leukemic human WBC, amphibia and reptiles: 2383
- squirrel herpesvirus, owl monkey or marmoset: 513, 2041, 2042
- surface membrane properties, transformed cells: 1326
- transplantation antigens, animal and human, review: 1009, 1442

VIRUS

- arbovirus
 - Cocal, effect on Friend leukemia virus splenomegaly, mouse: 2337
 - cytolytic effects, mouse leukemia cells: 2049
- cytoplasmic
 - amphibian tumors (frogs and newts): 2497
 - Lucké frog kidney tumors: 2495
 - and nuclear, Burkitt lymphoma biopsy specimens: 2478
- DNA-containing
 - effect on Shope fibroma virus, rabbit cells: 2476
- effect of aflatoxins, review: 2121
- exposure
 - liver cancer risk, international: 2561
 - perinatal and congenital leukemia, twins, review: 2136
- fish epidermal hyperplasia, properties: 323, 324
- foamy
 - latent infection, primate colony: 1276
 - type 1 (pseudomyxovirus), fusion of monkey kidney and SV20 adenovirus-induced hamster tumor cells: 1601
- formation, HeLa cells exposed to DNA from Hodgkin's disease lymph node: 1294
- fowl plague
 - effect of irradiation or actinomycin, singly- or doubly-infected cells: 780
- frog virus 3
 - effect on cellular DNA and RNA, human tumor (KB) cells: 2498
- hepatitis
 - Australia antigen, leukemia or Hodgkin's disease: 2591
 - Motol (human), synergism with diethyl-nitrosamine, hepatoma, mouse: 653
- human
 - lymphosarcoma cell line: 978
 - paramyxovirus, hamster screening: 518
 - picornavirus, hamster screening: 518
- infection
 - autoimmunity, cancer pathogenesis, review: 1025
 - time-space leukemia clusters, children, Japan: 126
- infectious parotitis
 - effect on defective Rous sarcoma virus: 1949

VIRUS (contd.)

- influenza
 - effect on urethan carcinogenesis, mouse: 1619, 2291
- insect densovirus (DNA virus)
 - transformation, mouse cells: 516
- lactate dehydrogenase-elevating (Riley agent)
 - induction of CNS symptoms, mouse: 103
- lymphocytic choriomeningitis
 - effect on autoimmunity, NZB mice: 2063
- measles
 - prevalence, leukemia clustering, children, Japan: 1675
- mouse hepatitis
 - replication, effect of mouse sarcoma virus *in vitro*: 111
- parainfluenza-like
 - isolation, (wild squirrels, Britain) and tumor induction (hamster): 1299
- paramyxo-like
 - effect on SV40 rescue, transformed hamster cells: 2508
- particles resembling
 - Bowen's disease of skin: 1295
 - carcinogen-induced brain tumors, review: 992
 - hamster melanoma: 82
 - intranuclear inclusion bodies, melanoma, human: 1292
 - methylcholanthrene-induced mouse brain tumor: 1297
 - plasmacytoma of frog with Lucké tumor transplant: 2496
- parvovirus H-1
 - effect on adenovirus-12-infected cells: 2004
- picodna (X-14 or H-1)
 - multiplication, effect of polyoma virus, rat embryo cells: 1271
- plant tumor
 - multiplication and cytopathology, insect: 321
- polio
 - infectivity, SV40-transformed human cells: 2454
- possible human tumor virus
 - cellular antibodies against HeLa cell antigen, human carcinomas: 751
- PR-8 myxovirus
 - immunization, effect on oncogenicity of lung cultures, hamster: 2462
- reo
 - infection, associated Gross-AKR leukemia virus infection, mouse: 757
 - intracellular membrane systems, Rous sarcoma virus-induced hamster tumors: 758
 - Type 3, Burkitt lymphoma, review: 2138
- RNA-containing
 - determinants of cancer, review: 8
 - effect on Shope fibroma virus, rabbit cells: 2476
 - particles resembling, human tumors: 1293
- RV-13 or 9HV-B rat virus
 - effect on Moloney (mouse) leukemia virus infection, rat: 101

VIRUS (contd.)

- Sendai
 - effect on
 - chromosomes and mitosis, hamster embryo cells: 317
 - defective Rous sarcoma virus: 1949
 - inactivated, effect on chick fibroblast-hamster Rous sarcoma heterokaryons and antigens: 2384
 - infection, immunosuppression, SV40 or adenovirus-16, hamster: 2418
 - irradiated, SV40 rescue, mixed mouse kidney-transformed mouse cell cultures: 852
 - transformed cells: 2435
 - Rous sarcoma virus rescue, mixed chick embryo-transformed hamster cell cultures: 786
- "slow" virus infection
 - Hodgkin's disease and multiple sclerosis, review: 2139
- superinfection of tumors: 869
- Type A particles
 - antibody-producing cells, autoimmune NZB mice: 2332
 - cell-transmitted mouse leukemia: 756
 - dimethylbenzanthracene-induced mouse thymoma: 76
 - methylcholanthrene-induced tumors, mouse: 1567, 1896
 - mineral oil-induced plasmacytoma: 730
 - ³²P-induced mouse leukemia: 1032
 - spontaneously-transforming mouse or rat embryo cells: 981
 - urethan + radiation-induced mouse thymic lymphoma: 75
 - mouse mammary tumor: 476, 2395
- Type A2 particles
 - urethan-induced leukemia or lung tumor, mouse: 1991
- Type B particles methylcholanthrene-induced ependymoblastoma, mouse: 822, 1567
- mouse mammary tumor: 476, 2395
- Type C particles
 - antibody-producing cells, autoimmune NZB mice: 2332
 - Bittner mouse mammary tumor virus-infected mouse cells: 1254
 - human breast cancer: 1600
 - mineral oil- or adjuvant-induced plasmacytoma, mouse: 1250, 1251, 1298
 - mouse mammary tumor: 476
 - pituitary mammatropic or mammosomatotropic tumors, rat: 2000
 - radiation-induced leukemia, mouse: 1032, 1203
 - spontaneously transformed mouse or rat embryo cells: 981
 - transplantable pigmented hamster melanoma: 1996
 - urethan-induced leukemia and lung tumor, mouse: 1991
- UV-HVJ
 - fusion of Ehrlich carcinoma and azaguanine-resistant L cells, properties of hybrid cells: 2499

VIRUS, ADENO-

- associated virus Types 1, 2 and 3
 - serum antibodies, human cancer: 2589
- bovine Type 3
 - isolation and properties of non-oncogenic variant, hamster: 2403
 - serum antibodies to T antigen, human cancer: 2588
- WB-PS variant, new antigens, infected hog kidney cells or hamsters: 2402
- canine A26/61 (respiratory-associated)
 - hamster tumors: 2006
- canine hepatitis
 - serum antibodies to T antigen, human cancer: 2588
- CELO (avian)
 - hamster tumors: 124, 2416
 - Petak or Phelps strain, hamster tumor cells, virus-specific tumor antigen: 2415
 - s.c. sarcoma or hepatoma (hamster) and T antigens (infected chick cells): 2511
 - transformed human cells, hamster tumors: 833
- human
 - DNA-RNA hybridization: 455, 514
- group A or B
 - serum antibodies, human cancer: 2588
 - virus-specific RNA, transformed cells: 1260
- group C
 - serum antibodies, human cancer: 2588
 - virus-specific RNA, transformed cells: 514, 1260
- Group D
 - properties: 484
 - mechanism of action, review: 1730
- oncogenic or nononcogenic, cytopathic effects, animal kidney cells: 872, 1259
- rodent tumors or transformed cells, nucleic acid homology studies, review: 2145
- SA-7 (simian)
 - brain tumors, hamster: 305, 2414
 - properties of cell line: 482
 - effect on SV40-transformed monkey kidney cells: 2438
 - hamster tumors, strain difference: 2412
 - transplantability, effect of SA-7 immunization: 1308
 - helper to human adenovirus-7, monkey kidney cells: 1329
 - infectivity and tumor induction (hamster), effect of UV irradiation: 1315
 - transformation, hamster or rat cells and hamster tumors: 485
- SA7(C8) simian
 - specific tumor immunity, hamster: 2413
- simian, subgroups I, II and III
 - serum antibodies to T antigen, human cancer: 2588
- SV5 (simian)
 - virus resembling, isolation and properties, Hodgkin's disease: 85
- SV11 (simian)
 - transformation (in vitro) and tumor induction (in vivo), hamster: 844

VIRUS, ADENO- (contd.)

- SV20 (simian)
 - abortive or productive infection, monkey or hamster kidney cells: 1602
 - hamster tumors, pathology: 123, 1601
- SV30 (simian)
 - effect on ultrastructure, monkey kidney cells: 1265
 - infected cells, ultrastructure: 2417
- Type 2
 - DNA denaturation pattern: 2059
 - endonuclease, infected hamster or human cells: 1320
 - effect on SV40 infection or transformation, monkey kidney cells: 2400, 2438
 - enhancement by SV40, monkey kidney cells: 2056
- SV40 hybrids
 - hamster tumor, nucleohistones: 486
 - nondefective strain, properties: 503
 - properties of viruses and transformed cells: 503, 2420, 2423, 2424, 2425, 2426
 - virus-specific RNA, infected or transformed cells: 835, 1260
- Type 3
 - cross-reacting tumor-specific transplantation antigens, mouse tumors: 2401
- Type 4
 - SV40 hybrid, transformation (hamster cells) and tumor induction (hamster): 1267
- Type 5
 - capsid proteins, synthesis and morphogenesis: 2055
 - effect on nuclear ultrastructure, human tumor cells: 2404
 - infected hamster cells, thymidine kinase: 836
 - Prague strain growth, HeLa cells: 306
- Type 7
 - cross-reactivity, mouse or hamster tumor: 121
 - effect on SV40-transformed monkey kidney cells: 2438
 - lași strain, growth, HeLa cells: 306
 - interaction with helper viruses (SV40 or SA-7), monkey kidney cells: 1329
 - oncogenic (hamster) strains, properties: 2005
 - serum antibodies, nasopharynx cancer, Hong Kong: 825
 - SV40 hybrids, properties: 2420, 2470
 - SV40(PARA) hybrids, properties of virus and transformed cells: 2419, 2421, 2422
 - transformation, cell growth kinetics, monkey kidney cells: 2470
 - virus-specific RNA, transformed cells: 1260
- Type 12
 - cross-reactivity, mouse or hamster tumor: 121
 - degradation and integration, abortively-infected hamster cells: 2057
- DNA
 - endonuclease, infected hamster or human cells: 1320

VIRUS, ADENO- (contd.)

- hybridization with Rous sarcoma virus RNA: 455
- effect on
 - benzpyrene carcinogenesis, hamster: 303, 1925
 - DNA, hamster cells: 2512
 - SV40-transformed monkey kidney cells: 2438
- group-specific T antigen, properties: 838
- infected human cells, antigens: 2408, 2411
- hamster tumors: 122, 483, 1603, 2405, 2407, 2409, 2412
- cellular antigens: 2407, 2408, 2411
- DNA composition: 1263
- effect of
 - liver extract from clam: 1310
 - phage or synthetic RNA: 840
 - fetal or newborn hamster: 873
 - intracellular tumor antigens: 1266
 - lipid composition: 1264
 - membrane transplantation antigen: 2003
 - nucleohistones, analysis: 486
 - tumor mitochondria-specific antigen: 788
- Huie strain, transplacental tumor induction, hamster: 1262
- induction of cellular DNA, human embryo cells: 837
- effect of parvovirus (H-1): 2004
- mouse tumors, antigens: 2401, 2411
- serum antibodies, human cancer: 304
- monkey: 2406
- nasopharynx cancer, Hong Kong: 825
- SV40 as helper, monkey kidney cells: 2445
- SV40 hybrid, transformed hamster cells, properties: 2423, 2424
- transformation, hamster cells: 839, 2002
- monkey kidney cells: 2410
- transformed gerbil cells, properties: 487
- virus-specific RNA, transformed cells: 1260
- Type 14
 - mouse tumors, tumor-specific transplantation antigens: 2401
- Type 16
 - effect on SV40 tumors, hamster: 2429
 - immunosuppression, Sendai virus-infected hamster: 2418
- Type 18
 - serum antibodies, human cancer: 834, 1261
 - virus-specific RNA, transformed cells: 1260
- Type 19
 - transformed hamster cells, hamster tumor induction: 484
- Type 26
 - transformed hamster cells, hamster tumor induction: 484
- Type 31
 - transforming efficiency, radiation effects, hamster embryo cells: 846
 - tumor-specific transplantation immunity, hamster: 845
 - virus-specific RNA, transformed cells: 1260

VIRUS, HERPES

- animal tumor viruses, classification, review: 9
 - cytomegalovirus
 - infection, complication of chemotherapy, human leukemia: 1612
 - Group 8, comparison to Marek's disease virus: 511
 - herpes simplex
 - attempted Epstein-Barr virus rescue, Burkitt lymphoma cells: 2061
 - effect on Shope fibroma virus, rabbit cells: 2476
 - genital or lip cancer, human, review: 2147
 - hamster screening: 518
 - persistent infection, mechanism, hamster cells: 824
 - rabbit antisera, comparison with Epstein-Barr virus antisera: 2480
 - replication, human lymphocytes: 1611
 - infected hamster cells, surface Forssman antigen: 1325
 - infection
 - age-related resistance, role of macrophages, mouse: 876
 - effect of silica or immune serum, mouse: 875
 - pre malignant lip neoplasms: 594
 - squirrel (*Herpesvirus saimiri*)
 - lymphoma induction, marmoset or owl monkey: 513, 2041, 2042
 - properties: 2040
 - Type 1
 - serum antibodies, cervix cancer: 2043
 - Type 1 or 2
 - effect on SV40-transformed monkey kidney cells: 2438
 - infection, cervix cancer, review: 9, 1721
 - serum antibodies, cervix cancer, Georgia (Atlanta): 2576
 - Type 2
 - distribution, Texas (Houston), venereal transmission: 510
 - serum antibodies, cervix cancer: 510, 2043
- VIRUS, HERPES-TYPE
- Epstein-Barr (human)
 - attempted rescue, herpes simplex virus: 2061
 - cell lines: 86, 301, 827, 828, 829, 830, 831, 1615, 1616, 1617, 2036, 2114
 - common antigen with Lucké virus: 2489
 - DNA, properties: 1257, 2034, 2035, 2479
 - human embryo cells, karyotype and virus replication: 297
 - induction of infectious mononucleosis, human cancer: 1643
 - infected cells, surface antigens: 1633
 - isolation, properties and distribution: 298, 299, 1255
 - morphology, Burkitt lymphoma biopsy specimens: 2478
 - nasopharynx cancer, Chinese and other Oriental populations, review: 1719
 - particulate debris on surface, WBC from pts. with leukemia or lymphoma: 1614

VIRUS, HERPES-TYPE (contd.)

- pathogenicity, human, review: 9, 1443, 2138, 2146, 2148
- rabbit antisera, comparison with herpes simplex antisera: 2480
- reaction with leukemia culture fluid-transformed human embryonic cells: 302
- serum antibodies
 - acute leukemia with infectious mononucleosis: 89, 2482
 - Burkitt lymphoma: 509, 826
 - cancer pts., West Germany (Essen): 2037
 - early viral antigens, human: 2481
 - infectious mononucleosis: 1613
 - intracellular and membrane antigen complexes: 2039
 - Japan (Akita Prefecture): 296
 - leukemia and lymphoma: 87
 - mammals and frogs: 2492
 - nasopharynx cancer: 523, 825, 826, 925, 2038
 - normal subjects, geographical distribution: 509, 523, 1256, 1616
 - transformation, human embryo cells: 298
 - virus-determined antigen receptors and species-specific membrane antigen sites: 300
- guinea pig
 - strain susceptible to L2C/NB leukemia: 1328
- human
 - cultures of nasopharynx cancer, Hong Kong (Chinese): 1632
 - embryonic cell lines transformed by leukemic cell extract, chromosomes: 88
 - isolation, Hodgkin's disease: 85
 - properties, leukemic WBC (QIMR-WIL) or Burkitt lymphoma cells (QIMR-GOR): 84
- leukovirus (human)
 - human WBC cell lines (normal, malignant or non-malignant diseases); 2631
- Lucké (frog)
 - associated cytoplasmic viral particles: 2495
 - attempted horizontal and vertical transmission: 2493
 - common antigen with Epstein-Barr virus: 2489
 - effect of temperature, tumor transplants: 2492
 - epidemiology of virus-positive tumors, Minnesota, North Dakota and Louisiana, seasonal changes: 2494
 - latent period, kidney tumors, frog: 2490
 - particles resembling, human prostate and breast cancer: 2044
- Marek's disease (chicken)
 - associated GA virus, chick liver tumor, enzymes: 1319
 - Biken A, B or C strain, nuclear or cytoplasmic inclusions, duck embryo cells: 2488
 - CAL-1 strain, properties: 91
 - comparison to cytomegalovirus group B: 511
 - effect of bromodeoxyuridine, chick or duck embryo cells: 2487

VIRUS, HERPES-TYPE (contd.)

- HPRS-16 strain, attenuation, chicken kidney cells: 832
- infection
 - effect of synthetic RNA polymer (polyinosinic-polycytidylic acid), chick: 512
 - serum immunoglobulins, chicken: 1258
 - isolation and properties: 877, 1618
- JM strain
 - cell-free transmission and replication, chick: 2486
 - cellular antigens, chick kidney cells: 2483
 - tissue antigens, infected or tumor-bearing chickens: 2484
 - viral antigen localization, host genetics, chicken: 508
 - morphogenesis and antigen formation, chick or duck embryo cells: 2485
 - review: 2149, 2150
 - RPL39 strain, tissue antigens, infected or tumor-bearing chickens: 2484
 - WSU-GF isolate, properties, chicken kidney cultures: 507
- VIRUS, HYBRID
 - adenovirus 2-SV40
 - properties of viruses and transformed cells: 486, 503, 2420, 2423, 2424, 2425, 2426
 - adenovirus 4-SV40
 - transformation, (hamster cells) and hamster tumor induction: 1267
 - adenovirus 7-SV40
 - properties: 2420, 2470
 - adenovirus 7-SV40(PARA)
 - properties: 2419, 2421, 2422
 - adenovirus 12-SV40
 - transformed hamster cells, properties: 2423, 2424
- VIRUS, LEUKEMIA/LYMPHOMA
 - AKR (mouse)
 - allogeneic leukemia induction, BALB mice: 1572
 - chemotherapy of spontaneous leukemias: 1573
 - gallium distribution, leukemic or non-leukemic AKR/J mice: 1775
 - immune virolysis: 2335
 - infection, effect of interferon, AKR mouse: 443
 - isolation, lymphoma (2731/L) from reovirus-infected mouse: 757
 - leukemic or preleukemic mice, host immunity: 1574
 - sensitivity, strain differences, mouse: 1983
 - spontaneous lymphoma, immunization, Gross leukemia virus induction, C57BL/6 mice: 1575, 1576
 - transmission, effect of germ-free status: 755
 - tumor pathology: 1228
 - AKR/J (mouse)
 - excretion, AKR/J, C58/J and SJL/J mice: 1979
 - animal, leukemia epidemiology, review: 578

VIRUS, LEUKEMIA/LYMPHOMA (contd.)

- avian
 - cytotropism, review: 1012
 - Rous lymphoma, Rous sarcoma virus replication, chick embryo cells: 1245
- avian leukosis
 - effect on defective Rous sarcoma virus: 1949
 - latent, detection, chick embryo cells: 793
 - particles resembling, calf kidney cell line: 752
 - spontaneous connective tissue tumor of snake (*Vipera russelli*): 471
 - properties: 870
 - subgroup A (RAV-1), interference with Rous sarcoma virus: 1947
 - subgroup B (RAV-2), interference with Rous sarcoma virus: 1947
 - subgroup C (RAV-50), interference with Rous sarcoma virus: 1947
 - virus-free colony of Japanese quail, reticulum cell sarcoma outbreak: 2051
- avian leukovirus
 - effect on infectious RSV(0) synthesis, chick embryo cells: 2385
- avian myeloblastosis
 - effect on Rous sarcoma virus production, chicken: 792
 - RNA, aminoacylation: 2054
 - viral RNA and complementary cellular DNA, leukemic chickens: 2378
- avian myeloblastosis-associated, subgroup B (MAV-2)
 - cellular DNA, preinfected chick embryo cells: 465
- avian myelomatosis
 - detection, chick cells: 783
- BAI strain A (avian myeloblastosis)
 - assay method, *in vitro* and chicken plasma: 464
 - effect on fowl plague virus replication, chick embryo cells: 780
 - group-specific antigen, chicken: 777
 - induction of tumor-specific transplantation antigens to Rous virus tumors, mouse: 789
 - leukemic WBC, effect of antitumor antibiotic: 1577
 - properties of non-transforming subgroups: 92
 - rabbit antibody complex, properties: 778
 - RNA and protein synthesis, infected blood cells, chick: 2377
 - RNA-dependent RNA polymerase, cells: 1230
 - transformed cells, properties of transfer RNA: 1995
- bovine leukosis
 - human leukemia epidemiology, Europe, review: 2135
- Bratislava-77 (avian myeloblastosis)
 - group-specific antigens, rat, chick or duckling tumors: 284
- 334C (mouse)
 - effect on
 - Friend virus pathogenicity, mouse: 1626
 - skin isograft survival, mouse: 1227
 - horizontal transmission: 2352

VIRUS, LEUKEMIA/LYMPHOMA (contd.)

- canine mast cell tumor
 - morphology: 282
- canine transmissible venereal tumor
 - review: 357
- chick erythroblastosis
 - induction of erythroblastosis or erythro-leukemia, rat: 754
- feline leukemia virus
 - antigen distribution, lymphosarcomas and other diseases, cats and other mammals: 447
 - complex with Moloney sarcoma virus, human leukemia virus indicator: 460
 - trans-specific infectivity: 459, 460
 - infectivity, human cells: 1965
 - propagation, human embryo cells: 760
 - properties: 104
 - trans-specific rescue of defective mouse sarcoma virus, hamster tumor cells: 449
 - Type C particles
 - detection and propagation: 105, 2390
 - myeloproliferative disorders, cat: 761
- feline syncytium-forming agent
 - isolation and properties: 448
- Friend (mouse)
 - age-related spontaneous remission, mouse: 1630
 - antibody formation, mouse, rat or rabbit: 1976
 - Axelrad strain (polycythemia- and splenic focus-inducing), immunosuppression, mouse: 2338
 - cell surface antigens: 1578
 - chloroma-inducing strain, pathogenicity, newborn mice: 1218
 - detection, method, mouse cell cultures: 1973
 - effect of
 - acetylenic carbamate, mouse: 265
- effect on
 - host immunity, sensitive or resistant mouse strains: 1570
 - mitochondrial enzymes, mouse spleen and liver: 1634
 - nucleases and nucleic acids, mouse spleen: 1571
 - skin isografts, mouse: 1227
 - splenic DNase and RNase, mouse: 765
 - transplanted rat tumors, mouse: 2344
 - rat: 2345
 - erythropoiesis, drug effects: 1568
 - F-S or F-B strains, identification of gene governing splenic focus formation: 2336
 - genetic susceptibility, bone marrow cells: 1217
 - mouse strains: 2339, 2340
 - group-specific antigen, properties: 435
 - horizontal transmission: 2352
 - immunosuppression, normal or tumor-bearing mouse: 766, 1972, 2064, 2338
 - infected mouse cells, effect of synthetic RNA polymer: 843
 - rat tumors, host immunity, rat: 764
 - infection, mouse: 96, 99, 436, 437, 1637, 1977, 2343

VIRUS, LEUKEMIA/LYMPHOMA (contd.)

- inhibitor, isolation, Rauscher leukemia virus-infected cell culture: 266, 1569
- interaction with interferon or interferon inducers, cell culture or mouse: 97, 451, 1235, 1321, 2346
- interference, Cocal arbovirus, mouse: 2337
- intracellular nuclease and nucleic acid, mouse spleen: 1306
- isolation, mouse chloroma: 264
- latent infection after suppression, mouse: 1971
- leukemogenesis, effect of synthetic RNA polymer, mouse: 841
- liver or spleen tetrahydrofolate dehydrogenase, mouse: 2350
- mouse tumor
 - inhibition by dimethylbenzanthracene: 617
 - pathology and disappearance of virus: 98, 106
- non-leukemogenic strain, properties: 268
- pathogenicity, inhibition by 334C mouse leukemia virus: 1626
- pathology of rat tumors: 100
- polycythemia-inducing strain, properties: 1974
- recovery (non-infectious reticulum cell sarcoma), Moloney leukemia virus as helper: 769
- replication, transplanted mouse tumor: 2342
- splenic focus-forming strains, properties: 1974, 1975
- susceptibility, effect of Rich virus-induced lymphoma, mouse: 2047
- transplantable rat tumor (WFT-2N), cellular immunity: 2341
- Friend-associated lymphatic leukemia virus (mouse)
 - effect on Friend leukemia virus splenomegaly, mouse: 436
- Friend-associated minimal pathogenicity virus (Rowson-Parr)
 - isolation and properties: 1215, 1216
- Graffi (mouse)
 - chromosomes, review: 1735
 - comparison of viral (structural) and cellular antigens: 762
 - isolation, spontaneous mouse sarcoma (RAB-1): 813
 - mouse lymphoma cells (GiC2 lymphoma), cellular antigens: 762
 - pathogenicity, newborn mice: 1223, 1224
 - pathology
 - and immunology in vivo: 263
 - tissue cultures: 2357
 - sarcoma, viral and cellular antigens: 271
 - tissue graft from resistant (XVII/G) to sensitive (C57BL) strain, leukemia induction: 1992
- Gross (mouse)
 - effect of immune sera or immunosuppressive agents, mouse: 102
 - effect on radiation leukemogenesis, rat: 2355
 - group-specific antigen, properties: 435

VIRUS, LEUKEMIA/LYMPHOMA (contd.)

- host immunity, mouse: 441, 1982
- induction, C57BL/6 mice immunized with AKR viral lymphoma cells: 1575, 1576
- infected mouse cells, effect of synthetic RNA polymer: 843
- intrathymic, accelerated leukemia: 1302
- isolation, lymphoma (2731/L) from reovirus-infected mouse: 757
- lymphoma induction, thymus graft, mouse: 1646
- particles resembling, radiation- or carcinogen-induced thymic lymphoma, mouse: 1203
- persistently-infected cell lines: 1309
- radiation promotion, rat: 20
- surface antigens: 2351, 2505
- transformed rat thymus cells, pathology: 2065
- transplantable lymphomas, syngeneic skin-graft rejection: 763
- guinea pig
 - cell-transmitted leukemia: 1644
- 9H rat leukemia virus
 - properties, heterogeneous virus population, rat embryo cells: 759
- human
 - attempted isolation, Hodgkin's disease cell line (AICHI-4): 267
 - indicator, Moloney sarcoma virus/feline leukemia virus complex: 460
 - leukemia epidemiology, review: 578, 586
 - mongolism with leukemia, review: 1026
 - particles resembling, non-lymphomatous lymph node hyperplasia: 1233
 - possible, leukemia clusters, Japan: 2095
 - review: 2146
 - screening, leukemic or normal blood or bone marrow: 83
 - transmission, mouse: 2502
 - virus-like particles, primates with transmitted human leukemic cells or filtered blood: 2503
- JM (avian leukosis)
 - serum antibodies, chicken: 319
- L2C (guinea pig)
 - pathogenicity, Strain 2 or hybrid guinea pig: 2633, 2634
- Mazurenko (mouse)
 - detection, mouse cell cultures: 1973
 - tissue antigens, mouse: 2354
- MC29 (avian leukosis)
 - effect on chicken bone marrow cells: 779
 - infected chick embryo cells, mesothelioma induction, chicken: 1994
- Moloney (mouse)
 - assay, mouse bone marrow cell line: 438
 - cell surface antigens, mouse lymphoma cultures: 446
 - comparison of viral (structural) and cellular antigens: 762
 - defective and competent, replication, mouse cells: 2359
 - effect on DNA and RNA, mouse embryo cells: 806

VIRUS, LEUKEMIA/LYMPHOMA (contd.)

- helper virus
 - recovery of Friend virus from non-infectious tumor: 769
 - from Moloney sarcoma-leukemia complex, isolation and properties: 1638
 - Moloney sarcoma virus-infected mouse or rat cells: 1247
- host immunity, rat: 439
- immunization by Harvey sarcoma virus, mouse: 279
- infected and tumor-inducing rat cell lines: 2356
- infection
 - effect of rat virus (RV-13 or 9HV-B), rat: 101
 - rescue of Moloney sarcoma virus from rat tumor (MSB-1), mouse: 804
- liver or spleen tetrahydrofolate dehydrogenase, mouse: 2350
- lymphoma antibodies, spleen, tumor-bearing mice: 770
- lymphosarcoma-inducing variant: 1620
- mouse lymphoma cells (YC2 lymphoma), cellular antigens: 762
- particles resembling, radiation- or urethan + radiation-induced mouse leukemia: 1459
- producer rat cell line, effect of extract on Friend viral leukemia (mouse): 1569
- rescue, MSV-33 rat-adapted sarcoma virus pseudotype: 1980
- RT34 rat strain, serum IgG, rat: 768
- surface antigens: 2351
- transformed cells, antigenic characterization: 108
- Moloney leukemia-sarcoma complex (mouse)
 - isolation and properties of helper virus: 1638
 - properties of RNA, transformed cells: 450
 - transformed rat cells (78A-1), bicatenoid RNA: 1246
 - serum IgG, infected rat: 1629
- Moloney M-MSV(FL) pseudotype (mouse)
 - effect of synthetic RNA polymer, Friend leukemia virus-infected cells: 451
- mouse
 - assay, method, mixed mouse embryo-Rous sarcoma virus-transformed rat cell cultures: 440
 - chloroleukemia, induction and transplantation: 1989
 - chromosomal anomalies, review: 1734
 - classification method: 2353
 - detection, lymphosarcoma of "starry-sky" histology: 1966
 - erythropoietic activity of leukemic cells: 1640
 - Friend-Moloney-Rauscher complex, comparison to Parma leukemia virus: 1234
 - genetic susceptibility, mechanism, NZB/NZW mouse: 444
 - role of hairless (hr) locus: 919
 - induction, sarcomas from irradiated cell cultures: 1752
 - infection, germ-free mice, review: 575

VIRUS, LEUKEMIA/LYMPHOMA (contd.)

- strain differences, mouse: 1305
- isolation, bones of high-leukemia mouse strains (AKR and C3H/Fg): 1981
- tumorigenic mouse embryo cell line: 442
- spontaneous leukemia of C58 mice, effect on CNS, mouse: 2331
- 6-mercaptopurine-induced lymphoma: 1552, 2389
- latent leukemia virus, high-plasma cell tumor mouse strain: 973
- leukemia-sarcoma complex
 - focus formation, mathematical model: 2333
 - sensitivity assay method: 2358
- methylcholanthrene-induced 6-mercaptopurine lymphoma: 1552
- myeloid chloroleukemia, effect on urethan carcinogenesis, mouse: 2288
- myeloid leukemia, isolation, methods: 1985, 1986
- tissue antigens, mouse: 1987
- occurrence, spontaneous ovarian or testicular teratomas, mouse: 1231
- particles resembling, calf kidney cell line: 752
- methylcholanthrene-induced mouse ependymblastoma: 1567, 1621
- mouse myeloma cells: 1988
- spontaneous kidney tumor, BALB/cf/Cd mice: 307
- strain-specific immunity disorders, NZB mice: 871
- possible activation, chemical carcinogens: 408
- mammary tumor virus, mouse: 2397
- properties and pathogenicity, chloroma: 264
- serum group-specific viral antibodies
 - high- or low-leukemia mouse strains: 2348
- mice or rats with methylcholanthrene-induced or viral sarcomas: 2348
- SJL/J reticulum cell neoplasms, transmission and biological activity: 1984
- ultrastructure, review: 579
- mouse erythroblastosis
 - infection, hemolytic anemia: 1566
 - interference with MSV-K sarcoma virus: 107
- Opler (guinea pig)
 - pathology of lymphoblastic leukemia: 1226
- Parma (mouse)
 - from Harvey sarcoma virus complex, properties: 1234
- radiation leukemia virus (mouse)
 - particles resembling, radiation- or carcinogen-induced thymic lymphoma, mouse: 1203
- radiation leukemia virus (rat)
 - antigenicity, rat lymphoma: 1628, 1636
- Type C virus particles, mouse or rat lymphoma: 1636
- Rauscher (mouse)
 - cell surface antigens: 1578, 2351
 - combined with diethylnitrosamine, transformation, rat embryo cells: 776

VIRUS, LEUKEMIA/LYMPHOMA (contd.)

- effect of
 - antitumor agent in vitro: 272
 - enzyme (L-asparaginase): 1579
 - interferon-inducing synthetic copolymer: 97
 - rabbit anti-mouse thymocyte serum: 1580
 - effect on
 - autoimmunity, NZB mice: 2048
 - lymphocytic stimulation response, mouse: 1978
 - mitochondrial enzymes, mouse spleen and liver: 1634
 - enhancement of Moloney virus sarcoma
 - in vivo: 270
 - G8-6 strain, propagation, human embryonic cells: 93
 - group-specific antigen, properties: 435
 - hamster tumor, properties of virus: 1220
 - HL-67-4 plasma virus, propagation, human embryonic cells: 93
 - horizontal transmission: 2352
 - immunosuppression, mouse: 262, 1219, 1318, 2347
 - induction of myelofibrosis with leukemia or lymphosarcoma, rat: 772
 - infected mouse cells
 - effect of synthetic RNA polymer: 843
 - isolation of Friend leukemia virus inhibitor: 1569
 - infection, mouse: 261, 1977
 - JLSV-5 cell line, extract with anti-Friend virus properties: 266
 - leukemia growth pattern, mouse: 775
 - liver or spleen tetrahydrofolate dehydrogenase, mouse: 2350
 - lymph node pathology, mouse: 2349
 - lymphoma cell line (#818), immunoglobulin production: 1582
 - particles resembling, radiation- or urethan + radiation-induced mouse leukemia: 1459
 - rat-adapted sarcoma virus pseudotype (MSV-33), rescue and virus-specific antigenicity: 1980
 - RNA synthesis, infected cells: 1944
 - RNA-dependent DNA polymerase: 1583
 - strain difference in susceptibility, mouse: 774
 - survival in atmospheric conditions: 1581
 - transformation, hamster cells: 94
 - transformed cells, properties: 260, 1221, 1222
 - transmission: 95
 - tumor pathology, mouse or rat: 771, 2046
 - virus-induced host immunity to syngeneic or allogeneic tumor cells, mouse: 773
- RadLV radiation leukemia virus
- loss of virus particles and specific surface antigen, rat: 445
 - sarcoma virus complex, focus formation, mouse embryo cells: 2334
- rat
- assay, method, mixed rat (Rous sarcoma virus-transformed) and mouse (embryonic) cell cultures: 440

VIRUS, LEUKEMIA/LYMPHOMA (contd.)

- rat-adapted strain of mouse erythroblastosis (MEV)
 - extrathymic lymphomas, rat: 753
 - rat leukemia
 - Type C particles: 1990
 - RAV-1 (avian lymphoma)
 - growth rate, infected cells: 269
 - Rich lymphoma (mouse)
 - effect on Friend leukemia virus susceptibility, mouse: 2047
 - rodent
 - cytotropism, review: 1012
 - RPL-12 avian lymphomatosis
 - avian leukosis-sarcoma group-specific antigens, chick embryo cells: 1586
 - T/S (mouse)
 - isolation (I_b line leukemia) and effect on CNS, age factors, mouse: 2331
- VIRUS, MAMMARY TUMOR
- Bittner (mouse)
- direct cell-to-cell transfer, C3H mouse mammary tumors: 1999
 - effect on growth rate, mouse kidney cells: 2394
 - infected mouse cells, release of leukemia virus particles: 1254
 - morphogenesis, spontaneous C3H mammary tumors: 2393
 - structure and properties: 1998
- cat
- spontaneous mammary carcinoma or adenocarcinoma: 1644
- human
- morphology, breast cancer: 293, 294, 295
 - mouse leukemia virus-like Type C particles: 1600
- milk agent (mouse)
- effect on transplanted mammary tumor: 28
- mouse
- absence of interferon-inducing or hemagglutinin activity: 823
 - activation, radiation or urethan, 020 strain mice: 818
 - agent-free strain (R111B/DE), incidence of mammary and other tumors: 554
 - Bittner and Mühlbock strains, interference: 115
 - blood activity, strain differences, mouse: 1593
 - centrifugation patterns: 2397, 2398
 - cross-reactivity with embryonic antigens, mouse: 2396
 - development of Type A particles: 287
 - distribution and milk antigenicity: 1252
 - effect on
 - DNA, hyperplastic alveolar nodules, mouse mammary gland: 1623
 - hormone-induced hyperplastic alveolar nodule outgrowth cell line (D1): 286
 - hyperplastic alveolar nodules: 819
 - skin, intramitochondrial dense bodies: 2184
 - high-MTV strain with low spontaneous mammary tumor incidence: 1253
 - high-tumor PBA strain: 2643

VIRUS, MAMMARY TUMOR (contd.)

- high-yield isolation method, C3H mouse milk: 478
- hormone effects in vivo: 116
- hyperplastic alveolar nodules, hormonal control of DNA synthesis: 292
- immunity: 285, 288
- infection and transmission, germ-free mice, review: 575
- infectivity, assay method, mouse: 1627
- isolation and properties: 290, 473, 474, 475, 2001
- nodule and tumor induction, effect of thymectomy: 820, 821
- particles resembling
 - calf kidney cell line: 752
 - spontaneous kidney tumor, BALB/cf/Cd mice: 307
- possible leukemia virus activation, mouse: 2397
- replication sequence: 477, 816, 817
- soluble antigens, virus from different mouse strains: 1595
- spleen cultures of infected mice, virus-associated surface antigens: 2399
- stimulation of production, tissue culture-to-newborn mouse or newborn rat, mouse tumor cell line: 1597
- structure: 480
- tissue immunity, virus-containing tissues of virus-free mice: 1596
- transfer RNA-methylating enzymes of tumor cells: 2647
- transmission: 114, 481, 1642
- tumor transplantation, virus-positive to virus-positive or virus-free strains: 1997
- ultrastructure, epithelial-mesenchymal junction: 349
- ultrastructure and production, mammary tumor cell cultures: 1594
- virus-containing tumors induced by Krebs-2 carcinoma cell DNA: 419
- virus-free mice, immunogenicity of spontaneous mammary tumors: 2053
- nodular outgrowths, effect of radiation or carcinogens: 1836

nodule-inducing virus (mouse)

- detection, mammary tumor virus-free strain and hybrids: 1599
- effect on
 - hormone-induced hyperplastic alveolar nodule cell line (D1): 286
 - hyperplastic alveolar nodules: 819
 - high- or low-prevalence mice, hyperplastic alveolar nodule frequency: 1622

rat

- dimethylbenzanthracene-, methylcholanthrene-, or diethylstilbestrol-induced mammary tumors: 1598, 2000

VIRUS, PAPOVA (papilloma-polyoma-vacuolating)

- bovine papilloma
 - meningeal and brain tumors, calf: 1268
 - serum precipitin response, cattle: 309
- transformation, hamster or mouse embryo cells: 491, 1270

VIRUS, PAPOVA (contd.)

- tumor pathology, cattle, horses and rodents: 1269
- canine oral papilloma virus
 - structure: 490
- canine papilloma
 - structure: 310
- equine papilloma
 - ultrastructure: 2472
- Graffi BB/T2 polyoma
 - rat tumors, standardization: 311
- hamster papovavirus
 - DNA, lymphoma-inducing effects, hamster: 488
- particles resembling
 - Wilms' tumor (child), transformed culture: 90
- polyoma
 - abortively infected cells, DNA and T antigen: 492
 - alkaline degradation patterns: 860
 - carrier population, mouse cells: 2464
 - CET strain and derivative (RTT) after mouse kidney passage, comparison: 863
 - DNA, effect on cellular genetics, mammalian cells, review: 2144
 - non-infectious supercoiled type: 861
 - effect of 6-methylmercaptopurine riboside, mouse embryo cells: 1625
 - effect on
 - antigen production, yeast culture: 1275
 - autoimmunity, NZB mice: 2063
 - DNA, mouse embryo cells: 117, 2467
 - morphology, mouse spleen: 1311
 - picodnavirus multiplication, rat embryo cells: 1271
 - hamster tumors: 497, 500, 855, 856, 862, 1272, 1608, 2013, 2016, 2017, 2058
 - host immunity, induction, antilymphocyte serum, mouse: 864
 - immunization, effect on oncogenicity of lung cultures, hamster: 2462
 - induction of chromosome replication, mouse cells: 493
 - infected cells: 318, 1273, 1325, 2012, 2014, 2018, 2463
 - infectivity, radiation effects, mouse cells: 855
 - large- or small-plaque strains, DNA ultrastructure: 2465
 - LID-1 VR 252 strain, host immunity and tumor development, hamster or mouse: 865
 - low-tumor clones, antigenicity, transformed hamster cells: 2011
 - mouse tumors: 2015, 2457
 - particles resembling, progressive multifocal leukoencephalopathy and chronic leukemia, case: 2471
 - propagation in fungi: 322
 - properties of virion: 2008
 - rabbit fibrosarcoma cell lines, properties: 867
 - rat tumors: 311, 866, 2348
 - RBC receptors, human: 2466
 - replication of ring-shaped DNA, mouse embryo cells: 494

VIRUS, PAPOVA (contd.)

- Rowe strain, hamster tumor extract, specific polyoma virus repressor: 854
- runting, effect of immune serum, hamster: 2058
- specific inhibitor, infected hamster cells: 498
- strain 3049/PIB₂, capsid antigen, infected mouse cells: 2458
- surface antigens, infected or transformed cells: 1273, 1324, 1325
- synergism with fluorenylacetamide, rat: 1202
- temperature-sensitive mutant, properties: 2009
- thermosensitive mutant (Ts-a), transformed cells, properties: 2468, 2469
- Toronto strain (small-plaque)
 - effect on mouse-hamster somatic hybrid cells: 2461
 - transformation, hamster brain cells: 2460
- transformation, hamster cells: 2470
 - mechanism, review: 10
 - odontogenic epithelium, mouse embryo: 1274
- transformed cells: 312, 401, 499, 500, 580, 1324, 2010, 2019, 2060, 2432, 2459
- UV sensitivity of target areas: 496
- viral genome transcription, mouse cells: 495
- Shope papilloma (rabbit)
 - cellular immunity and serum-mediated inhibition of immunity: 308
 - masking, mechanism, rabbit tumors: 2007
 - mitotic activity during keratinization, rabbit tumor: 2473
 - properties of virion: 2008
 - skin tumor induction, mechanism, rabbit: 1609
 - spontaneously regressing papillomas, rat: 1327
 - surface antigen, papilloma cells: 489
- SV40
 - adenovirus-2 hybrid
 - hamster tumor, nucleohistone analysis: 486
 - nondefective strain (AD.2⁺ND₁), properties: 503
 - properties of viruses and transformed cells: 2420, 2423, 2424, 2425, 2426
 - adenovirus-4 hybrid
 - transformation (hamster cells) and tumor induction (hamster): 1267
 - adenovirus-5 enhancement, monkey kidney cells: 2056
 - adenovirus-7 hybrids
 - properties: 2420, 2470
 - adenovirus-12 hybrids
 - transformed cells, properties: 2423, 2424
 - capsid proteins, analysis: 2031
 - cellular antigens, detection method: 119
 - coat protein antigens, nonpermissive nuclei of heterokaryocyte cultures: 1277
 - defective (PARA)
 - adenovirus-7 hybrids, properties: 2419, 2421, 2422
 - transformation, mouse cells: 2028

VIRUS, PAPOVA (contd.)

- DNA
 - cleavage, bacterial endonuclease: 2506
 - hybridization: 455, 1280
 - replication, monkey kidney cells: 2437, 2439, 2447
 - transformation, human cells: 851
- effect of nitrosoguanidine compound: 2033
- effect on
 - adenovirus-2 infection, monkey cells: 2400
 - human thyroid cells: 1284
- gene activity, lytic infection, monkey kidney cells: 501
- hamster tumors: 500, 788, 842, 845, 850, 1281, 1316, 1323, 1603, 1606, 1631, 2021, 2023, 2029, 2431
- helper for adenovirus, monkey kidney cells: 1329, 2445
- immunosuppression, hamster: 767, 2418
- infected cells, animal or human: 318, 849, 874, 1286, 1641, 2018, 2020, 2427, 2441, 2442, 2443, 2444, 2449, 2509
- infection, monkey: 118, 1276, 2440
- monkey-mouse hybrid cell lines with viral genome: 1278
- mutagenesis and tumor induction, Drosophila: 517
- mutants
 - isolation of double lysogens from transformed cells: 1279
 - properties of DNA: 1289
- polio vaccine, neonatal vaccination, cancer incidence in childhood: 316
- pseudovirions, detection and properties, monkey cells: 2032, 2447
- radiation effects, infected cells or hamster: 1751
- replication
 - effect of repressor from polyoma virus-induced hamster tumor, monkey cells: 854
 - radiation effects, monkey kidney cells: 857
- rescue: 504, 852, 2435, 2452, 2508
- serum antibodies, children with leukemia or solid tumors, polio vaccination: 1605
- human cancer: 304
- rabbit: 2428
- specific repressor, abortively or productively infected cells: 853
- strain A426
 - hamster tumors, effect of adenovirus-16: 2429
 - T antigen, mammalian cells, species differences: 2450
- transformation
 - hamster cells: 846, 1282, 1285
- transformation
 - human cells: 120, 2434, 2451, 2454, 2470
 - mechanism, review: 10
 - monkey cells: 2025, 2026, 2027, 2451, 2470
 - mouse cells: 2358, 2470
 - species difference, rodent cells: 2430
 - susceptibility, high-leukemia family: 1225

VIRUS, PAPOVA (contd.)

XX/XXY mosaic cells from pt. with
Klinefelter's syndrome and lung cancer:
2456

transformed cells, animal or human: 313,
314, 315, 401, 500, 501, 502, 505, 506,
580, 847, 848, 858, 859, 1283, 1287, 1288,
1300, 1317, 1322, 1323, 1324, 1604, 1607,
1639, 2019, 2022, 2024, 2062, 2431, 2432,
2433, 2436, 2438, 2446, 2448, 2453, 2455,
2507, 2510

tumorigenic mouse cell lines, ganglioside
types: 515

tumorigenicity (hamster), effect of anti-
tumor agents: 1641

UV-irradiated, hamster tumors, transplantation
immunity: 1631

VIRUS, POX

myxoma

effect on Shope fibroma virus, rabbit cells:
2476

Shope fibroma (rabbit)

cellular immunity, measurement, infected
rabbit cells: 2474

DNA, isolation and properties: 1610

in vitro titration: 1291

Patuxent strain

cellular DNA, effect of radiation or
contact inhibition, rabbit cells:
2475

effect of other viruses, rabbit cells:
2476

vaccinia

effect on Shope fibroma virus, rabbit cells:
2476

reactivation of Yaba monkey virus: 868

verruca vulgaris (human)

epidermodysplasia verruciformis with malign-
ant transformation, case: 2501

Yaba histiocytoma (monkey)

adaptation and growth kinetics, monkey
kidney cells: 2477

inactivation (heat or UV) and reactivation
(vaccinia virus): 868

isolation (testis tumors of monkeys) and
properties: 1290

monkey tumors, ribonucleotide reductase
activity: 125

VIRUS, SARCOMA

avian

subgroups B, C and D, effect of polyanions
and polycations: 782

subgroups C and D, properties and classifi-
cation: 781

B77 (avian)

rat-adapted strain, properties: 1963

temperature-sensitive mutants, properties:
1962

transformation, rat cells: 1963

cat

C-type, isolation and pathogenicity:
1964

infectivity, human cells: 1965

cat fibrosarcoma

transmission, marmoset: 2504

transplacental, cat or dog: 2392

VIRUS, SARCOMA (contd.)

Claude's CTV-10 (chicken)

virus titer and effect of amputation, chicken:
2379

FBJ osteosarcoma (mouse)

classification: 814

infection, hamster or rat: 814

transformation, rat embryo cells: 472

tumor induction, strain differences, mouse:
814

Finkel osteosarcoma (mouse)

replication and transformation, rat embryo
cells: 1314

Friend M-MSV(FLV) pseudotype (mouse)

tumor development, effect of synthetic RNA
polymer, mouse: 461

Friend pseudotype (mouse)

sarcoma, effect of synthetic RNA polymer,
mouse: 1303

Graffi pseudotype (mouse)

comparison of viral (structural) and cellu-
lar antigens: 762

Gross pseudotype (mouse)

transformed mouse embryo cells, carbohydrate
uptake: 463

hamster

reticulum cell sarcoma: 2052

hamster-specific

C-type virus, isolation, Moloney (Gross
pseudotype) sarcoma virus-induced hamster
tumor: 802

isolation, hamster tumor induced by Kirsten
(mouse) sarcoma virus: 801

Harvey (mouse)

defective, rescue (feline leukemia virus),
hamster tumor cells: 449

effect of

immune sera, mouse or rat: 109

Plasmodium berghei yoelii infection, mouse:
1960

hamster tumors: 811, 2362, 2364

immunization against Moloney leukemia virus,
mouse: 279

infected cells, effect of DNA antimetabolite:
1958

mouse tumors

immunogenicity: 1248

pathology: 281, 1957, 2363

virus yield: 1957

properties of Parma leukemia virus from com-
plex: 1234

rat osteosarcoma: 811, 2364

sugar transport, infected or transformed
cells: 2360

transformed cells, properties: 108, 280, 463,
809, 810, 1959, 1961, 2361

tumor growth kinetics, theoretical model:
2050

human

bone or soft tissue sarcoma cultures: 468,
815, 1592

isolation (serum or tumor from women with
ovarian tumors) and tumorigenicity (chick):
1645

serum antibodies, sarcoma pts. and their
relatives: 815, 1591

VIRUS, SARCOMA (contd.)

Kirsten (mouse)
 hamster-specific virus, isolation, hamster sarcoma: 458, 801
 rescue (feline leukemia virus), hamster tumor cells: 449
 transformed human cells, properties: 812
 Mill Hill-2 reticuloendothelioma (chicken)
 classification and genetic resistance: 1950
 Moloney (mouse)
 competent populations, isolation and properties: 452, 807
 defective
 feline leukemia virus complex, trans-specific infectivity: 459, 460
 properties: 452, 807, 1247
 Rauscher leukemia virus from hamster tumor as helper: 1220
 replication, mouse cells: 2359
 rescue, hamster tumor cells: 449, 2369
 DNA, RNA and enzyme activities, mouse rhabdomyosarcoma: 1590
 effect of
 antitumor agents, in vitro or in vivo: 272, 808, 1589, 1635, 1956
 interferon inducer, cell culture: 1235
 synthetic RNA polymer, Friend leukemia virus-infected cells: 451
 effect on
 DNA and RNA, mouse embryo cells: 806
 mouse hepatitis virus replication in vitro: 111
 enhancement, Rauscher virus, in vivo: 270
 Gross pseudotype, hamster tumor, hamster-specific sarcoma virus: 802
 hamster tumor (T-MSV), interferon-antagonistic factors: 462
 immunosuppression, mouse: 2370
 immunotherapy: 808, 1589
 infected cells, loss of interferon response, mechanism: 805
 infection
 effect of inhibitor, mouse: 1977
 and tumor development, kinetics, newborn mouse: 1304
 interference, non-leukemogenic Friend virus strain: 268
 M-MSV(MLV) pseudotype, effect of synthetic RNA polymer on tumor development, mouse: 461
 osteosarcoma, hamster or rat: 811
 replication, human cells (WI-38 cell line): 1624
 rescue from rat tumor (MSB-1), Moloney leukemia virus-infected mouse: 804
 transformed cells: 108, 110, 809, 810, 812, 1955, 2361, 2366
 effect of antitumor agents: 803, 1956
 tumor growth kinetics, theoretical model: 2050
 tumor pathology
 chick or rodent: 2365
 hamster: 2362, 2364, 2365
 mouse: 281, 1957, 2363, 2365, 2367
 rat: 2364, 2365, 2368

VIRUS, SARCOMA (contd.)

Moloney pseudotype (mouse)
 comparison of viral (structural) and cellular antigens: 762
 sarcoma induction, effect of synthetic RNA polymer: 1303
 Moloney sarcoma-leukemia complex (mouse)
 isolation and properties of helper virus: 1638
 properties of RNA, transformed cells: 450, 1246
 serum IgG, infected rat: 1629
 mouse
 effect of synthetic RNA polymer, mouse embryo cells: 843
 isolation and properties, Sarcoma #37: 283
 leukemia-sarcoma complex
 focus formation, mathematical model: 2333
 sensitivity assay method: 2358
 lymphosarcoma-inducing variant of Moloney leukemia virus: 1620
 pseudotype of radiation leukemia virus, leukemia virus complex, focus formation, mouse embryo cells: 2334
 spontaneous tumors, chemotherapy, SJL/J mice: 1573
 transformed cells, effect of serum growth factor: 2436
 MSV-33 pseudotype (rat)
 rescue and virus-specific antigenicity: 1980
 MSV-K (mouse)
 interference, mouse erythroblastosis virus: 107
 Rauscher pseudotype (mouse)
 transformation, quantitation, hamster cells: 809
 transformed mouse embryo cells, carbohydrate uptake: 463
 Rous (chicken)
 #559 strain
 mutagenesis and tumor induction, Drosophila: 517
 APL-22 strain
 serum antibodies, domestic and wild birds, USSR: 2382
 Bryan strain
 avian leukosis-sarcoma group-specific antigens, infected cells or tumors: 1586
 cellular DNA, preinfected chick embryo cells: 465
 defective, effect of Rous-associated or avian leukosis virus: 1949
 hamster tumors, reovirus particles: 758
 infectivity, wild and domestic birds: 1239
 nonviral growth-stimulating factor in medium, chick embryo cells: 791
 phenotypically mixed populations: 785
 replication, synchronized cells: 1941
 resistance, chick embryo cells: 2376
 RNA, hybridization, DNA of viral and cellular (mammalian, plant, bacterial or yeast) origin: 455
 serum antibodies, domestic and wild birds, USSR: 2382

VIRUS, SARCOMA (contd.)

- transformed cells: 1313, 1942, 2374, 2387
- tumor induction and mutagenesis, *Drosophila*: 517
- Carr-Zilber strain
 - mouse-adapted, properties: 277, 278
 - mouse tumors, mouse variant virus: 2372
 - pathology: 2371
 - serum antibodies, domestic and wild birds, USSR: 2382
 - tumor induction, strain differences, rat: 1585
- DNA synthesis stimulation, mechanism, human cells: 456
- effect of
 - carcinogens, chick: 52
 - rifampicin, chick embryo cells: 794
- effect on
 - DNA and RNA, infected or transformed chick embryo cells: 2386
 - nucleic acids and growth, chick embryo cells: 276
- Engelbreth-Holm strain
 - serum antibodies, domestic and wild birds, USSR: 2382
 - transformed human cells (EH-118MG), properties: 1951
- Harris strain
 - avian leukosis-sarcoma group-specific antigens, chick embryo cells: 1586
 - defective, properties: 1948
 - interference with RSV-b(0): 1947
- exposure, tumor development, dexamethasone-treated baboon: 457
- growth rate of infected cells: 269
- hamster tumors: 273, 466, 800, 1237, 2375, 2384
- immunization, avian leukosis-sarcoma group-specific serum antibodies, chickens or turkeys: 1586
- inactivation, heat or ether: 113
- infected chick embryo cells, nuclear fragmentation: 795
- infection, effect of synthetic RNA polymer, chick: 512
- latent infection, detection, chick embryo cells: 793
- monkey sarcoma, attempted virus unmasking: 1307
- mouse-adapted strain
 - hamster tumor induction: 277
- mouse tumors
 - karyotype: 112
 - leukemia virus group-specific antigen: 2348
- particles resembling, calf kidney cell line: 752
- Prague strain
 - group-specific antigen components, infected cells: 777
 - mouse tumors, properties: 1952
- production, mixed mammalian-chick embryo cell cultures: 274
- properties of tumor cell DNA, chick: 2648
- rat tumors
 - effect of histidine decarboxylase inhibitors on protein synthesis: 1243

VIRUS, SARCOMA (contd.)

- group-specific tumor antigens: 284, 2348
- RBI rat sarcoma, tumor induction, hamster: 1587
- RNA, possible subunit structure: 784
- RNA-dependent DNA polymerase: 1583
- RSV(0)
 - cell-associated factor required for synthesis of infectious virus, chick embryo cells: 2385
 - effect of polyanions and polycations: 782
 - envelope properties: 1943
 - helper virus-free, infectivity, birds: 1946
- RSV-B(0)
 - helper virus-free, interference with avian leukosis viruses: 1947
- RSV(RAV-1) pseudotype
 - phenotypically mixed populations: 785
 - RNA synthesis, infected cells: 1944
 - transformation, effect of medium, chick embryo cells: 1945
- Schmidt-Ruppin strain
 - avian leukosis-sarcoma group-specific antigens, infected or tumor cells: 1586
 - brain tumors, dog: 797, 1240
 - detection, chick cells: 783
 - enhanced virus production, chicken: 792
 - group-specific antigen components, infected cells: 777
 - hamster tumors: 799, 1236, 1238, 1586
 - infected chicken-mouse mixed cell cultures, tumor induction, mouse: 1241
 - infectivity, wild and domestic birds: 1239
 - kinetics of Type A and C particle development, transformed chicken cells: 787
 - leukemoid reaction, conventional or germ-free rat: 1301, 1953
 - mouse tumors: 453, 788, 1242, 1952, 1954
 - mouse variants: 2372
 - mutagenesis, radiation, chick embryo: 2381 and tumor induction, *Drosophila*: 517
 - rat tumors: 1236, 1244, 1301, 2373
 - replication, Rous avian lymphoma-infected cells, DNA synthesis: 1245
 - rescue (Sendai virus), mixed chick embryo-transformed hamster cell cultures: 786
 - RNA and protein synthesis, chick embryo cells: 454
 - RNA-dependent DNA polymerase in virions: 2388
 - serum antibodies, domestic and wild birds, USSR: 2382
 - soft tissue or bone sarcomas, marmoset: 798
 - transformed cells: 466, 1312, 1584, 1588
 - tumor induction
 - amphibia and reptiles: 2383
 - rat: 790, 1585
 - serum antibodies, human cancer: 304
 - strain D
 - replication, chick embryo cells: 2380
 - transformation, monkey kidney cells: 275
 - transformed cells
 - effect of nitrogen mustard derivative, rat: 796

VIRUS, SARCOMA (contd.)

- hamster embryo, fowl plague virus multipli-
cation, cellular DNA: 780
- rat, mixed-culture bioassay for leukemia
viruses: 440
- tumor-specific transplantation antigens, in-
duction, avian myeloblastosis virus,
mouse: 789
- Rous-associated (chicken)
effect on defective Rous sarcoma virus: 1949
- RAV-1
Bryan high-titer strain, detection, in-
fected cells: 783
- group-specific antigen, properties, in-
fected cells: 777
- infected chick embryo cells, enzymes:
1588
- RAV-2
infected chick embryo cells, enzymes:
1588
- subgroups A, B, C and D, cellular DNA, pre-
infected cells: 465
- Rous-interference factor (chicken)
detection of latent avian leukosis virus
infection, chick embryo cells: 793
- ST fibrosarcoma (cat)
tumor induction, marmoset: 1249
- pathology and Type C particles, kitten:
2391

VITAMIN A

- effect on benzpyrene-induced squamous meta-
plasia, hamster trachea in vitro: 1795

VITAMIN A PALMITATE

- effect on
benzpyrene-induced lung and forestomach
tumors, hamster: 1089
- dimethylbenzanthracene cheek pouch tumors,
hamster: 694
- lymphoma-like tumors, hamster cheek pouch:
1164

VITAMIN B2 (See Riboflavin)

VITAMIN B6 (See Pyridoxine)

VITAMIN E

- effect on skin carcinogenesis, mouse: 1486

WATER POLLUTION

- benzanthracene, petrochemical effluents,
analytical method: 1827

WATER POLLUTION (contd.)

- benzpyrene
method of removal: 1788
- review: 2116
- polycyclic aromatic hydrocarbons, analysis,
method: 1785
- skin papillomas, fish, San Francisco Bay: 534

WATER SUPPLY

- annual rainfall, cancer distribution, U.S.:
1647
- chlorination, screening of chlorinated benz-
pyrene derivatives, mouse: 602
- trace metal content, cancer incidence, Italy
(Pesaro): 2072

WAX, MEDICINAL

- ozokerite ceresin (from USSR), carcinogen con-
tent and skin carcinogenesis (mouse): 2307

WOOD

- occupational exposure, ethmoid sinus tumors:
367
- smoke
drying method, effect on benzpyrene content
of prunes: 2215
- effect on benzpyrene content of fish: 2209

XANTHINE, 3-HYDROXY-

- effect on DNase-II, cell-free system: 612
- s.c. tumors
mouse: 1161
- rat: 1161, 1189
- urinary metabolites, rat: 618

XANTHURENIC ACID 8-METHYL ETHER

- metabolism
mouse: 71
- rabbit: 1932

YABA VIRUS (See under Virus, pox)

YOHIMBINE

- effect on dimethylaminoazobenzene hepatoma,
rat: 206

ZINC

- serum, hepatoma, South Africa (Bantus): 202
- and tissues, lung and other cancer, human:
1135

ZINC DIMETHYLDITHIOCARBAMATE

- lung tumors, mouse: 1778

ZINC ETHYLENE-BIS(DITHIOCARBAMATE)

- lung tumors, mouse: 1778

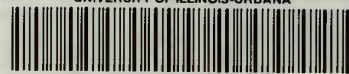
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